

=> file biosis caba caplus lifesci medline

=> e liu jun/au

```
E1      2      LIU JUMMING/AU
E2      1      LIU JUMN HUA/AU
E3      3793 --> LIU JUN/AU
E4      9      LIU JUN AN/AU
E5      1      LIU JUN ANG/AU
E6      1      LIU JUN BAO/AU
E7      4      LIU JUN BIN/AU
E8      2      LIU JUN BING/AU
E9      21     LIU JUN BO/AU
E10     1      LIU JUN CHANG/AU
E11     6      LIU JUN CHAO/AU
E12     1      LIU JUN CHEN/AU
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=> s e3 and BCG

L1 11 "LIU JUN"/AU AND BCG

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 4 DUP REM L1 (7 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

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L2  ANSWER 1 OF 4  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
    DUPLICATE 1
AN  2008:84494  BIOSIS <<LOGINID::20080329>>
DN  PREV200800088178
TI  Differential productions of lipid virulence factors among  ***BCG***
    vaccine strains and implications on  ***BCG***  safety.
AU  Chen, Jeffrey M.; Islam, Salim T.; Ren, Huiping;  ***Liu, Jun***
    [Reprint Author]
CS  Univ Toronto, Dept Med Genet and Microbiol, 4382 Med Sci Bldg,1 Kings Coll
    Circle, Toronto, ON M5S 1A8, Canada
    jun.liu@utoronto.ca
SO  Vaccine, (NOV 23 2007) Vol. 25, No. 48, pp. 8114-8122.
    CODEN: VACCDE. ISSN: 0264-410X.
DT  Article
LA  English
ED  Entered STN: 23 Jan 2008
    Last Updated on STN: 23 Jan 2008
AB  Safety of  ***BCG***  is a major concern in countries with a high burden
    of HIV/AIDS. Current  ***BCG***  vaccine comprises of a heterogeneous
    group of substrains showing genotypic differences. The impact of these
    differences on  ***BCG***  efficacy and safety remains unknown. Here we
    show that three  ***BCG***  substrains,  ***BCG***  -Japan, -Moreau,
    and -Glaxo, do not produce phthiocerol dimycocerosates (PDIMs) and
    phenolic glycolipids (PGLs), two cell wall lipids known to be important
    for the virulence of Mycobacterium tuberculosis and Mycobacterium bovis,
    suggesting that these  ***BCG***  strains are more attenuated than
    others. We found that there is a good correlation between the ability of
    ***BCG***  strains to produce these two lipids and the propensity of
    ***BCG***  to induce complications following vaccination in children,
    which provides a partial explanation for the molecular mechanisms of
    ***BCG***  reactogenicity. Our finding has important implications for
    national immunization programmes particularly in HIV endemic countries.
```

We suggest that PDIMs/PGLs analysis could offer a practical means for assessing the safety of various ***BCG*** vaccine strains currently used in the world. (c) 2007 Elsevier Ltd. All rights reserved.

TI Differential productions of lipid virulence factors among ***BCG*** vaccine strains and implications on ***BCG*** safety.

AU Chen, Jeffrey M.; Islam, Salim T.; Ren, Huiping; ***Liu, Jun***
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IT . . .
disease, infectious disease, immune system disease, AIDS
Acquired Immunodeficiency Syndrome (MeSH)

IT Chemicals & Biochemicals
lipid; phenolic glycolipid; Bacillus Calmette-Guerin vaccine [
BCG vaccine]: immunologic-drug, efficacy, safety

L2 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2

AN 2004:338289 BIOSIS <<LOGINID::20080329>>

DN PREV200400338470

TI Impact of methoxymycolic acid production by mycobacterium bovis
BCG Vaccines.

AU Belley, Adam; Alexander, David; Di Pietrantonio, Tania; Girard, Manon;
Jones, Joses; Schurr, Erwin; ***Liu, Jun*** ; Sherman, David R.; Behr,
Marcel A. [Reprint Author]

CS Div Infect Dis and Med Microbiol, Montreal Gen Hosp, 1650 Cedar Ave,
Montreal, PQ, H3G 1A4, Canada
marcel.behr@mcgill.ca

SO Infection and Immunity, (May 2004) Vol. 72, No. 5, pp. 2803-2809. print.
ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 11 Aug 2004
Last Updated on STN: 11 Aug 2004

AB ***BCG*** vaccines are a family of closely related daughter strains of an attenuated isolate of Mycobacterium bovis derived by in vitro passage from 1908 to 1921. During subsequent laboratory propagation of the vaccine strain until its lyophilization in 1961, ***BCG*** Pasteur underwent at least seven further genomic mutations. The impact of these mutations on the properties of the vaccine is currently unknown. One mutation, a glycine-to-aspartic acid substitution in the mmaA3 gene,

occurred between 1927 and 1931 and impairs methoxymycolic acid synthesis in ***BCG*** strains obtained from the Pasteur Institute after this period. Mycolic acids of the cell wall are classified into three functional groups (alpha-, methoxy-, and ketomycolic acids), and together these lipids form a highly specialized permeability barrier around the bacterium. To explore the impact of methoxymycolic acid production by ***BCG*** strains, we complemented the functional gene of *mmaA3* into ***BCG*** Denmark and tested a number of in vitro and in vivo phenotypes. Surprisingly, restoration of methoxymycolic acids alone had no effect on cell wall permeability, resistance to antibiotics, or growth in cultured macrophages and C57BL/6 mice. Our results demonstrate that the loss of methoxymycolic acid production did not apparently affect the virulence of ***BCG*** strains.

TI Impact of methoxymycolic acid production by *Mycobacterium bovis* ***BCG*** Vaccines.

AU Belley, Adam; Alexander, David; Di Pietrantonio, Tania; Girard, Manon; Jones, Joses; Schurr, Erwin; ***Liu, Jun*** ; Sherman, David R.; Behr, Marcel A. [Reprint Author]

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IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection

IT Chemicals & Biochemicals
methoxymycolic acid: ***BCG*** vaccine production, vaccine response impact

ORGN . . .
Vertebrates

ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
Bacteria; Microorganisms

Organism Name
Mycobacterium bovis (species) [***BCG*** (common)]: pathogen,
immune response, vaccine

Taxa Notes
Bacteria, Eubacteria, Microorganisms

L2 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:855955 CAPLUS <<LOGINID::20080329>>

DN 139:363579

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine dehydratase
 and/or glutamine synthetase
 IN ***Liu, Jun*** ; Chen, Jeffrey; Alexander, David
 PA Can.
 SO PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003089462	A2	20031030	WO 2003-CA566	20030416
	WO 2003089462	A3	20040521		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2481108	A1	20031030	CA 2003-2481108	20030416
	AU 2003218838	A1	20031103	AU 2003-218838	20030416
	GB 2403477	A	20050105	GB 2004-25165	20030416
	GB 2403477	B	20060823		
	CN 1703513	A	20051130	CN 2003-802276	20030416
	JP 2006508633	T	20060316	JP 2003-586182	20030416
	ZA 2004008344	A	20050907	ZA 2004-8344	20041014
	US 2007264286	A1	20071115	US 2006-511718	20060728
PRAI	US 2002-372450P	P	20020416		
	WO 2003-CA566	W	20030416		

AB The invention relates to a live recombinant Mycobacterium bovis-
 BCG strain comprising a nucleic acid capable of expression, the
 nucleic acid encoding at least one protein or polypeptide that exhibits
 alanine dehydrogenase activity, glutamine synthetase activity, or serine
 dehydratase activity. The recombinant alanine dehydrogenase, serine
 dehydratase and glutamine synthetase are derived from Mycobacterium
 tuberculosis.

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine dehydratase
 and/or glutamine synthetase

IN ***Liu, Jun*** ; Chen, Jeffrey; Alexander, David

AB The invention relates to a live recombinant Mycobacterium bovis-
 BCG strain comprising a nucleic acid capable of expression, the
 nucleic acid encoding at least one protein or polypeptide that exhibits.

ST recombinant Mycobacterium bovis ***BCG*** strain tuberculosis vaccine;
 alanine dehydrogenase serine dehydratase glutamine synthetase ***BCG***
 tuberculosis vaccine

IT Immunostimulants
 (adjuvants; tuberculosis vaccines including recombinant Mycobacterium
 bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Drug delivery systems

(carriers; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT Proteins
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (recombinant; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT Antitumor agents
 Bladder, neoplasm
 Bos taurus
 Culture media
 DNA sequences
 Human
 Mammalia
 Molecular cloning
 Mycobacterium
 Mycobacterium ***BCG***
 Mycobacterium tuberculosis
 Pathogen
 Protein sequences
 Test kits
 Tuberculosis
 Vaccines
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT Gene, microbial
 Nucleic acids
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT Antigens
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-18-5P 619345-20-9P 619345-21-0P 619345-22-1P 619345-23-2P 619345-24-3P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-19-6
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-25-4P 619345-27-6P 619345-28-7P 619345-29-8P 619345-30-1P
619345-31-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(nucleotide sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-26-5, DNA (Mycobacterium bovis gene ald)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(nucleotide sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 7440-44-0, Carbon, biological studies 7727-37-9, Nitrogen, biological
studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(source; tuberculosis vaccines including recombinant Mycobacterium
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT 9014-27-1P, Serine dehydratase 9023-70-5P, Glutamine synthetase
9029-06-5P, Alanine dehydrogenase 175380-16-2P, GenBank Z70692
193398-67-3P, GenBank Z97193 196526-70-2P, GenBank U87280
199902-12-0P, GenBank AL008883 202943-88-2P, GenBank AL021428
335511-06-3P, GenBank AE006919 335512-36-2P, GenBank AE007049
335512-60-2P, GenBank AE007073 335513-04-7P, GenBank AE007117
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT 50-99-7, Dextrose, biological studies 56-41-7, L-Alanine, biological
studies 56-45-1, L-Serine, biological studies 56-81-5, Glycerol,
biological studies 71-00-1, L-Histidine, biological studies 77-92-9,
Citric acid, biological studies 338-69-2, D-Alanine 7439-89-6, Iron,
biological studies 7439-95-4, Magnesium, biological studies
14808-79-8, Sulfate, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

L2 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 3

AN 2003:127824 BIOSIS <<LOGINID::20080329>>

DN PREV200300127824

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and
serine catabolism.

AU Chen, Jeffrey M.; Alexander, David C.; Behr, Marcel A.; ***Liu, Jun***
[Reprint Author]

CS Department of Medical Genetics and Microbiology, University of Toronto, 1
King's College Circle, 4382 Medical Sciences Building, Toronto, ON, M5S
1A8, Canada
jun.liu@utoronto.ca

SO Infection and Immunity, (February 2003) Vol. 71, No. 2, pp. 708-716.
print.
ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-alanine dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***-Pasteur and ***BCG***-Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine within the host.

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AU Chen, Jeffrey M.; Alexander, David C.; Behr, Marcel A.; ***Liu, Jun***
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IT . . .
disease
Tuberculosis, Pulmonary (MeSH)

IT Diseases
tuberculosis: bacterial disease
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
D-alanine; L-alanine; L-alanine dehydrogenase; L-serine; Mycobacterium bovis ***BCG*** vaccines: immunologic-drug, immunostimulant-drug; glutamine synthetase [EC 6.3.1.2]

=> e chen jeffrey/au

E1 1 CHEN JEFFERY J/AU
E2 2 CHEN JEFFERY K/AU
E3 39 --> CHEN JEFFREY/AU
E4 19 CHEN JEFFREY C/AU
E5 1 CHEN JEFFREY CHUANG FEI/AU
E6 4 CHEN JEFFREY E/AU
E7 6 CHEN JEFFREY E K/AU
E8 1 CHEN JEFFREY F/AU
E9 15 CHEN JEFFREY J/AU
E10 2 CHEN JEFFREY L/AU
E11 20 CHEN JEFFREY M/AU
E12 1 CHEN JEFFREY S/AU

=> s e1-e12 and BCG

L3 7 ("CHEN JEFFERY J"/AU OR "CHEN JEFFERY K"/AU OR "CHEN JEFFREY"/AU
OR "CHEN JEFFREY C"/AU OR "CHEN JEFFREY CHUANG FEI"/AU OR "CHEN
JEFFREY E"/AU OR "CHEN JEFFREY E K"/AU OR "CHEN JEFFREY F"/AU
OR "CHEN JEFFREY J"/AU OR "CHEN JEFFREY L"/AU OR "CHEN JEFFREY
M"/AU OR "CHEN JEFFREY S"/AU) AND BCG

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 3 DUP REM L3 (4 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 2008:84494 BIOSIS <<LOGINID::20080329>>
DN PREV200800088178
TI Differential productions of lipid virulence factors among ***BCG***
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AU ***Chen, Jeffrey M.*** ; Islam, Salim T.; Ren, Huiping; Liu, Jun
[Reprint Author]
CS Univ Toronto, Dept Med Genet and Microbiol, 4382 Med Sci Bldg, 1 Kings Coll
Circle, Toronto, ON M5S 1A8, Canada
jun.liu@utoronto.ca
SO Vaccine, (NOV 23 2007) Vol. 25, No. 48, pp. 8114-8122.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 23 Jan 2008
Last Updated on STN: 23 Jan 2008
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 which provides a partial explanation for the molecular mechanisms of
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 and -Glaxo, do not produce phthiocerol dimycocerosates (PDIMs) and
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 for the virulence of Mycobacterium tuberculosis and Mycobacterium bovis,
 suggesting that these ***BCG*** strains are more attenuated than
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 BCG strains to produce these two lipids and the propensity of
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 which provides a partial explanation for the molecular mechanisms of
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 national immunization programmes particularly in HIV endemic countries.
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IT . . .
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 Acquired Immunodeficiency Syndrome (MeSH)

IT Chemicals & Biochemicals
 lipid; phenolic glycolipid; Bacillus Calmette-Guerin vaccine [
 BCG vaccine]: immunologic-drug, efficacy, safety

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:855955 CAPLUS <<LOGINID::20080329>>
 DN 139:363579
 TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine dehydratase
 and/or glutamine synthetase

IN Liu, Jun; ***Chen, Jeffrey*** ; Alexander, David
 PA Can.
 SO PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003089462	A2	20031030	WO 2003-CA566	20030416
	WO 2003089462	A3	20040521		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA	2481108	A1	20031030	CA	2003-2481108	20030416
AU	2003218838	A1	20031103	AU	2003-218838	20030416
GB	2403477	A	20050105	GB	2004-25165	20030416
GB	2403477	B	20060823			
CN	1703513	A	20051130	CN	2003-802276	20030416
JP	2006508633	T	20060316	JP	2003-586182	20030416
ZA	2004008344	A	20050907	ZA	2004-8344	20041014
US	2007264286	A1	20071115	US	2006-511718	20060728
PRAI	US 2002-372450P	P	20020416			
WO	2003-CA566	W	20030416			

AB The invention relates to a live recombinant *Mycobacterium bovis*-
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 dehydratase and glutamine synthetase are derived from *Mycobacterium*
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TI Tuberculosis vaccines including recombinant *Mycobacterium bovis*-
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IN Liu, Jun; ***Chen, Jeffrey*** ; Alexander, David

AB The invention relates to a live recombinant *Mycobacterium bovis*-
 BCG strain comprising a nucleic acid capable of expression, the
 nucleic acid encoding at least one protein or polypeptide that exhibits.

. .

ST recombinant *Mycobacterium bovis* ***BCG*** strain tuberculosis vaccine;
 alanine dehydrogenase serine dehydratase glutamine synthetase ***BCG***
 tuberculosis vaccine

IT Immunostimulants
 (adjuvants; tuberculosis vaccines including recombinant *Mycobacterium*
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Drug delivery systems
 (carriers; tuberculosis vaccines including recombinant *Mycobacterium*
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Proteins
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (recombinant; tuberculosis vaccines including recombinant *Mycobacterium*
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Antitumor agents
 Bladder, neoplasm
Bos taurus
 Culture media
 DNA sequences
 Human
 Mammalia

Molecular cloning
 Mycobacterium
 Mycobacterium ***BCG***
 Mycobacterium tuberculosis
 Pathogen
 Protein sequences
 Test kits
 Tuberculosis
 Vaccines
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Gene, microbial
 Nucleic acids
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT Antigens
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT 619345-18-5P 619345-20-9P 619345-21-0P 619345-22-1P 619345-23-2P
 619345-24-3P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (amino acid sequence; tuberculosis vaccines including recombinant
 Mycobacterium bovis- ***BCG*** strains expressing alanine
 dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-19-6
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (amino acid sequence; tuberculosis vaccines including recombinant
 Mycobacterium bovis- ***BCG*** strains expressing alanine
 dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-25-4P 619345-27-6P 619345-28-7P 619345-29-8P 619345-30-1P
 619345-31-2P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (nucleotide sequence; tuberculosis vaccines including recombinant
 Mycobacterium bovis- ***BCG*** strains expressing alanine
 dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-26-5, DNA (Mycobacterium bovis gene ald)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (nucleotide sequence; tuberculosis vaccines including recombinant
 Mycobacterium bovis- ***BCG*** strains expressing alanine
 dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 7440-44-0, Carbon, biological studies 7727-37-9, Nitrogen, biological
 studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
 (source; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 9014-27-1P, Serine dehydratase 9023-70-5P, Glutamine synthetase
 9029-06-5P, Alanine dehydrogenase 175380-16-2P, GenBank Z70692
 193398-67-3P, GenBank Z97193 196526-70-2P, GenBank U87280
 199902-12-0P, GenBank AL008883 202943-88-2P, GenBank AL021428
 335511-06-3P, GenBank AE006919 335512-36-2P, GenBank AE007049
 335512-60-2P, GenBank AE007073 335513-04-7P, GenBank AE007117
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

IT 50-99-7, Dextrose, biological studies 56-41-7, L-Alanine, biological
 studies 56-45-1, L-Serine, biological studies 56-81-5, Glycerol,
 biological studies 71-00-1, L-Histidine, biological studies 77-92-9,
 Citric acid, biological studies 338-69-2, D-Alanine 7439-89-6, Iron,
 biological studies 7439-95-4, Magnesium, biological studies
 14808-79-8, Sulfate, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing alanine dehydrogenase, serine
 dehydratase and/or glutamine synthetase)

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 DUPLICATE 2

AN 2003:127824 BIOSIS <<LOGINID::20080329>>

DN PREV200300127824

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and
 serine catabolism.

AU ***Chen, Jeffrey M.*** ; Alexander, David C.; Behr, Marcel A.; Liu, Jun
 [Reprint Author]

CS Department of Medical Genetics and Microbiology, University of Toronto, 1
 King's College Circle, 4382 Medical Sciences Building, Toronto, ON, M5S
 1A8, Canada
 jun.liu@utoronto.ca

SO Infection and Immunity, (February 2003) Vol. 71, No. 2, pp. 708-716.
 print.
 ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 5 Mar 2003
 Last Updated on STN: 5 Mar 2003

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the
 prevention of tuberculosis (TB) in humans. ***BCG*** is a live
 vaccine, and induction of immunity to TB requires productive infection of
 the host by ***BCG***. However, ***BCG*** is not a satisfactory
 vaccine, because it fails to protect against pulmonary TB in adults. In
 this study, we found that ***BCG*** strains cannot utilize many
 naturally occurring amino acids as the sole nitrogen source for growth.
 This defect is caused, at least partially, by the lack of functional
 metabolic enzymes. All ***BCG*** strains are unable to catabolize
 L-alanine or D-alanine due to a frameshift mutation in the L-alanine

dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***
 -Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine,
 apparently due to inadequate expression of L-serine deaminase (sdaA). We
 also found that undegraded alanine and serine inhibit the growth of
 BCG through blockage of glutamine synthetase. These results
 suggest that ***BCG*** strains are limited in nitrogen metabolic
 capacity and predict defects that may restrict multiplication and
 persistence of the live vaccine within the host.

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and
 serine catabolism.

AU ***Chen, Jeffrey M.*** ; Alexander, David C.; Behr, Marcel A.; Liu, Jun
 [Reprint Author]

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the
 prevention of tuberculosis (TB) in humans. ***BCG*** is a live
 vaccine, and induction of immunity to TB requires productive infection of
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 vaccine, because it fails to protect against pulmonary TB in adults. In
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 This defect is caused, at least partially, by the lack of functional
 metabolic enzymes. All ***BCG*** strains are unable to catabolize
 L-alanine or D-alanine due to a frameshift mutation in the L-alanine
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 -Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine,
 apparently due to inadequate expression of L-serine deaminase (sdaA). We
 also found that undegraded alanine and serine inhibit the growth of
 BCG through blockage of glutamine synthetase. These results
 suggest that ***BCG*** strains are limited in nitrogen metabolic
 capacity and predict defects that may restrict multiplication and
 persistence of the live vaccine. . .

IT . . .
 disease
 Tuberculosis, Pulmonary (MeSH)

IT Diseases
 tuberculosis: bacterial disease
 Tuberculosis (MeSH)

IT Chemicals & Biochemicals
 D-alanine; L-alanine; L-alanine dehydrogenase; L-serine; Mycobacterium
 bovis ***BCG*** vaccines: immunologic-drug, immunostimulant-drug;
 glutamine synthetase [EC 6.3.1.2]

=> e alexander david/au

E1	2	ALEXANDER DAVE B/AU
E2	8	ALEXANDER DAVE M/AU
E3	74 -->	ALEXANDER DAVID/AU
E4	31	ALEXANDER DAVID A/AU
E5	1	ALEXANDER DAVID ALAN/AU
E6	1	ALEXANDER DAVID ALLEN/AU
E7	1	ALEXANDER DAVID ANDREW/AU
E8	1	ALEXANDER DAVID AUSTIN/AU
E9	36	ALEXANDER DAVID B/AU
E10	1	ALEXANDER DAVID BEDELL/AU
E11	1	ALEXANDER DAVID BRUCE/AU
E12	57	ALEXANDER DAVID C/AU

=> s e1-12 and BCG

L5 15 ("ALEXANDER DAVE B"/AU OR "ALEXANDER DAVE M"/AU OR "ALEXANDER
DAVID"/AU OR "ALEXANDER DAVID A"/AU OR "ALEXANDER DAVID ALAN"/AU
OR "ALEXANDER DAVID ALLEN"/AU OR "ALEXANDER DAVID ANDREW"/AU
OR "ALEXANDER DAVID AUSTIN"/AU OR "ALEXANDER DAVID B"/AU OR "ALE
XANDER DAVID BEDELL"/AU OR "ALEXANDER DAVID BRUCE"/AU OR "ALEXAN
DER DAVID C"/AU) AND BCG

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 6 DUP REM L5 (9 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1

AN 2007:564157 BIOSIS <<LOGINID::20080329>>

DN PREV200700566212

TI Rv1773 is a transcriptional repressor deleted from ***BCG*** -Pasteur.

AU ***Alexander, David C.*** ; Behr, Marcel A. [Reprint Author]

CS Montreal Gen Hosp, Div Infect Dis and Med Microbiol, 1650 Cedar Ave,
Montreal, PQ H3G 1A4, Canada
marcel.behr@mcgill.ca

SO Tuberculosis (Amsterdam), (SEP 2007) Vol. 87, No. 5, pp. 421-425.
ISSN: 1472-9792.

DT Article

LA English

ED Entered STN: 31 Oct 2007

 Last Updated on STN: 31 Oct 2007

AB Mycobacterium bovis Bacille Calmette-Guerin (***BCG***) is a live
attenuated vaccine for the prevention of tuberculosis. Transcriptome
comparison reveals dyregulated expression of two genes, Rv1774 and Rv1775,
exclusively in the Pasteur strain of ***BCG*** . We show that these
genes form a bicistronic operon regulated by Rv1773, a transcriptional
repressor deleted during the in vitro evolution of ***BCG*** . (c) 2007
Elsevier Ltd. All rights reserved.

TI Rv1773 is a transcriptional repressor deleted from ***BCG*** -Pasteur.

AU ***Alexander, David C.*** ; Behr, Marcel A. [Reprint Author]

AB Mycobacterium bovis Bacille Calmette-Guerin (***BCG***) is a live
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genes form a bicistronic operon regulated by Rv1773, a transcriptional
repressor deleted during the in vitro evolution of ***BCG*** . (c) 2007
Elsevier Ltd. All rights reserved.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1033917 CAPLUS <<LOGINID::20080329>>

DN 145:395457

TI Improved tuberculosis vaccine containing a start codon mutation in the
.sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains

IN Behr, Marcel; Mostowy, Serge; Charlet, Danielle; ***Alexander, David***

PA McGill University, Can.

SO PCT Int. Appl., 74pp.

 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006102767	A1	20061005	WO 2006-CA503	20060403
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	CA 2603298	A1	20061005	CA 2006-2603298	20060403
	EP 1863914	A1	20071212	EP 2006-721759	20060403
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRAI US 2005-667243P P 20050401
WO 2006-CA503 W 20060403

AB The present invention relates to an improved tuberculosis (TB) vaccine and further includes a method for detg. the potency of TB strains. Mycobacterium bovis Bacille Calmette-Guerin (***BCG***) strains are genetically and phenotypically heterogeneous. Expression of the antigenic proteins MPB70 and MPB83 is known to vary considerably across ***BCG*** strains; however, the reason for this phenotypic difference has remained unknown. Because the history of ***BCG*** strain dissemination has been recorded, it has been possible to precisely det. the chronol. of specific genetic changes in ***BCG*** strains. A no. of these mutations affect putative regulatory genes, so it was hypothesized that a mutation in a regulatory gene was likely responsible for the variable prodn. of MPB70 and MPB83. The prodn. of MPB70 and MPB83 across a panel of ***BCG*** strains was therefore detd., in order to assign the chronol. of this phenotypic change and thereby guide studies towards identifying the responsible mutation. Interestingly, the data implicate a start codon mutation in the M. tuberculosis .sigma.K factor (Rv0445c or sigK gene) and point to a highly specific link between sigK and expression of MPB70 and MPB83.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Improved tuberculosis vaccine containing a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains
IN Behr, Marcel; Mostowy, Serge; Charlet, Danielle; ***Alexander, David***
AB . . . improved tuberculosis (TB) vaccine and further includes a method for detg. the potency of TB strains. Mycobacterium bovis Bacille Calmette-Guerin (***BCG***) strains are genetically and phenotypically heterogeneous. Expression of the antigenic proteins MPB70 and MPB83 is known to vary considerably across ***BCG*** strains; however, the reason for this phenotypic difference has remained unknown. Because the history of ***BCG*** strain dissemination has been recorded, it has been possible to precisely det. the chronol. of specific genetic changes in ***BCG*** strains. A no. of these mutations affect putative regulatory genes, so it was hypothesized that a mutation in a regulatory. . . likely responsible for the variable prodn. of MPB70 and MPB83. The prodn. of MPB70 and MPB83 across a panel of ***BCG*** strains was

therefore detd., in order to assign the chronol. of this phenotypic change and thereby guide studies towards identifying. . .

ST sigmaK gene mutation Mycobacterium ***BCG*** tuberculosis vaccine; antigenic protein MPB70 MPB83 expression sigma factor Mycobacterium; sequence gene sigK transcription factor mutation Mycobacterium

IT Antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (MPB70; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (MPB83; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Bison
 Bos taurus
 Capra
 Cervidae
 DNA microarray technology
 DNA sequences
 Elk
 Human
 Mammalia
 Molecular cloning
 Mutation
 Mycobacterium ***BCG***
 Mycobacterium africanum
 Mycobacterium bovis
 Mycobacterium canettii
 Mycobacterium caprae
 Mycobacterium microti
 Mycobacterium pinnipedii
 Mycobacterium tuberculosis
 Ovis aries
 Protein sequences
 Sus scrofa domestica
 Tuberculosis
 Vaccines
 (improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Probes (nucleic acid)
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Gene, microbial
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sigK; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Genetic polymorphism
 (single nucleotide; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT Transcription factors

RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.sigma.K; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT 911336-42-0 911336-44-2
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amino acid sequence; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT 911336-41-9, DNA (Mycobacterium ***BCG*** gene sigK) 911336-43-1
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nucleotide sequence; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

IT 911336-48-6 911336-49-7 911336-50-0 911336-51-1 911336-52-2
 911336-53-3 911336-54-4 911336-55-5 911336-56-6 911336-57-7
 911336-58-8 911336-59-9 911336-60-2 911336-61-3 911336-62-4
 911336-63-5 911336-64-6 911336-65-7 911336-66-8 911336-67-9
 911336-68-0 911336-69-1 911336-70-4 911336-71-5 911336-72-6
 911336-73-7 911336-74-8 911336-75-9 911336-76-0 911336-77-1
 911336-78-2 911336-79-3 911336-80-6 911336-81-7 911336-82-8
 911336-83-9 911336-84-0 911336-85-1 911336-86-2 911336-87-3
 911336-88-4 911336-89-5 911336-90-8 911336-91-9 911336-92-0
 911336-93-1 911336-94-2 911336-95-3 911336-96-4 911336-97-5
 911336-98-6
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; improved tuberculosis vaccine contg. a start codon mutation in the .sigma. factor gene sigK of Mycobacterium bovis ***BCG*** strains)

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 2

AN 2005:273753 BIOSIS <<LOGINID::20080329>>

DN PREV200510060685

TI Reduced expression of antigenic proteins MPB70 and MPB83 in Mycobacterium bovis ***BCG*** strains due to a start codon mutation in sigK.

AU Charlet, Danielle; Mostowy, Serge; ***Alexander, David*** ; Sit, Louis; Wiker, Harald G.; Behr, Marcel A. [Reprint Author]

CS McGill Univ, Dept Med, Div Expt Med, Montreal, PQ, Canada
 marcel.behr@mcgill.ca

SO Molecular Microbiology, (JUN 2005) Vol. 56, No. 5, pp. 1302-1313.
 CODEN: MOMIEE. ISSN: 0950-382X.

DT Article

LA English

ED Entered STN: 21 Jul 2005
 Last Updated on STN: 21 Jul 2005

AB Mycobacterium bovis Bacille Calmette-Guerin (***BCG***) strains are genetically and phenotypically heterogeneous. Expression of the antigenic proteins MPB70 and MPB83 is known to vary considerably across ***BCG*** strains; however, the reason for this phenotypic difference has remained unknown. By immunoblot, we separated ***BCG*** into high- and low-producing strains. By quantitative reverse transcription polymerase chain reaction (RT-PCR), we determined that transcription of the antigen-encoding genes, mpb70 and mpb83, follows the same strain pattern

with mRNA levels reduced over 50-fold in low-producing strains. Transcriptome comparison of the same ***BCG*** strains by DNA microarray revealed two gene regions consistently downregulated in low-producing strains compared with high-producing strains, one including mpb70 (Rv2875) and mpb83 (Rv2873) and a second that includes the predicted sigma factor, sigK. DNA sequence analysis revealed a point mutation in the start codon of sigK in all low-producing ***BCG*** strains. Complementation of a low-producing strain, ***BCG*** Pasteur, with wild-type sigK fully restored MPB70 and MPB83 production. Microarray-based analysis and confirmatory RT-PCR of the complemented strains revealed an upregulation in gene transcription limited to the sigK and the mpb83/mpb70 gene regions. These data demonstrate that a mutation of sigK is responsible for decreased expression of MPB70 and MPB83 in low-producing ***BCG*** strains and provide clues into the role of Mycobacterium tuberculosis SigK.

TI Reduced expression of antigenic proteins MPB70 and MPB83 in Mycobacterium bovis ***BCG*** strains due to a start codon mutation in sigK.

AU Charlet, Danielle; Mostowy, Serge; ***Alexander, David*** ; Sit, Louis; Wiker, Harald G.; Behr, Marcel A. [Reprint Author]

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L6 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 3

AN 2004:338289 BIOSIS <<LOGINID::20080329>>

DN PREV200400338470

TI Impact of methoxymycolic acid production by mycobacterium bovis ***BCG*** Vaccines.

AU Belley, Adam; ***Alexander, David*** ; Di Pietrantonio, Tania; Girard, Manon; Jones, Joses; Schurr, Erwin; Liu, Jun; Sherman, David R.; Behr, Marcel A. [Reprint Author]

CS Div Infect Dis and Med Microbiol, Montreal Gen Hosp, 1650 Cedar Ave, Montreal, PQ, H3G 1A4, Canada
marcel.behr@mcgill.ca

SO Infection and Immunity, (May 2004) Vol. 72, No. 5, pp. 2803-2809. print. ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 11 Aug 2004
 Last Updated on STN: 11 Aug 2004

AB ***BCG*** vaccines are a family of closely related daughter strains of an attenuated isolate of *Mycobacterium bovis* derived by in vitro passage from 1908 to 1921. During subsequent laboratory propagation of the vaccine strain until its lyophilization in 1961, ***BCG*** Pasteur underwent at least seven further genomic mutations. The impact of these mutations on the properties of the vaccine is currently unknown. One mutation, a glycine-to-aspartic acid substitution in the *mmaA3* gene, occurred between 1927 and 1931 and impairs methoxymycolic acid synthesis in ***BCG*** strains obtained from the Pasteur Institute after this period. Mycolic acids of the cell wall are classified into three functional groups (alpha-, methoxy-, and ketomycolic acids), and together these lipids form a highly specialized permeability barrier around the bacterium. To explore the impact of methoxymycolic acid production by ***BCG*** strains, we complemented the functional gene of *mmaA3* into ***BCG*** Denmark and tested a number of in vitro and in vivo phenotypes. Surprisingly, restoration of methoxymycolic acids alone had no effect on cell wall permeability, resistance to antibiotics, or growth in cultured macrophages and C57BL/6 mice. Our results demonstrate that the loss of methoxymycolic acid production did not apparently affect the virulence of ***BCG*** strains.

TI Impact of methoxymycolic acid production by *mycobacterium bovis* ***BCG*** Vaccines.

AU Belley, Adam; ***Alexander, David*** ; Di Pietrantonio, Tania; Girard, Manon; Jones, Joses; Schurr, Erwin; Liu, Jun; Sherman, David R.; Behr, Marcel A. [Reprint Author]

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IT Major Concepts
 Immune System (Chemical Coordination and Homeostasis); Infection

IT Chemicals & Biochemicals
 methoxymycolic acid: ***BCG*** vaccine production, vaccine response impact

ORGN . . .
 Vertebrates

ORGN Classifier
 Mycobacteriaceae 08881
 Super Taxa
 Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
 Bacteria; Microorganisms

Organism Name

Mycobacterium bovis (species) [***BCG*** (common)]: pathogen,
immune response, vaccine

Taxa Notes

Bacteria, Eubacteria, Microorganisms

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:855955 CAPLUS <<LOGINID::20080329>>

DN 139:363579

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine dehydratase
and/or glutamine synthetase

IN Liu, Jun; Chen, Jeffrey; ***Alexander, David***

PA Can.

SO PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2003089462	A2	20031030	WO 2003-CA566	20030416
	WO 2003089462	A3	20040521		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2481108	A1	20031030	CA 2003-2481108	20030416
	AU 2003218838	A1	20031103	AU 2003-218838	20030416
	GB 2403477	A	20050105	GB 2004-25165	20030416
	GB 2403477	B	20060823		
	CN 1703513	A	20051130	CN 2003-802276	20030416
	JP 2006508633	T	20060316	JP 2003-586182	20030416
	ZA 2004008344	A	20050907	ZA 2004-8344	20041014
	US 2007264286	A1	20071115	US 2006-511718	20060728
PRAI	US 2002-372450P	P	20020416		
	WO 2003-CA566	W	20030416		

AB The invention relates to a live recombinant Mycobacterium bovis-
BCG strain comprising a nucleic acid capable of expression, the
nucleic acid encoding at least one protein or polypeptide that exhibits
alanine dehydrogenase activity, glutamine synthetase activity, or serine
dehydratase activity. The recombinant alanine dehydrogenase, serine
dehydratase and glutamine synthetase are derived from Mycobacterium
tuberculosis.

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine dehydratase
and/or glutamine synthetase

IN Liu, Jun; Chen, Jeffrey; ***Alexander, David***

AB The invention relates to a live recombinant Mycobacterium bovis-
BCG strain comprising a nucleic acid capable of expression, the
nucleic acid encoding at least one protein or polypeptide that exhibits.

ST recombinant Mycobacterium bovis ***BCG*** strain tuberculosis vaccine;
alanine dehydrogenase serine dehydratase glutamine synthetase ***BCG***
tuberculosis vaccine

IT Immunostimulants
(adjuvants; tuberculosis vaccines including recombinant Mycobacterium
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT Drug delivery systems
(carriers; tuberculosis vaccines including recombinant Mycobacterium
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(recombinant; tuberculosis vaccines including recombinant Mycobacterium
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT Antitumor agents
Bladder, neoplasm
Bos taurus
Culture media
DNA sequences
Human
Mammalia
Molecular cloning
Mycobacterium
Mycobacterium ***BCG***
Mycobacterium tuberculosis
Pathogen
Protein sequences
Test kits
Tuberculosis
Vaccines
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT Gene, microbial
Nucleic acids
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or glutamine synthetase)

IT 619345-18-5P 619345-20-9P 619345-21-0P 619345-22-1P 619345-23-2P
619345-24-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(amino acid sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-19-6
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-25-4P 619345-27-6P 619345-28-7P 619345-29-8P 619345-30-1P 619345-31-2P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 619345-26-5, DNA (Mycobacterium bovis gene ald)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (nucleotide sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 7440-44-0, Carbon, biological studies 7727-37-9, Nitrogen, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (source; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 9014-27-1P, Serine dehydratase 9023-70-5P, Glutamine synthetase
 9029-06-5P, Alanine dehydrogenase 175380-16-2P, GenBank Z70692
 193398-67-3P, GenBank Z97193 196526-70-2P, GenBank U87280
 199902-12-0P, GenBank AL008883 202943-88-2P, GenBank AL021428
 335511-06-3P, GenBank AE006919 335512-36-2P, GenBank AE007049
 335512-60-2P, GenBank AE007073 335513-04-7P, GenBank AE007117
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

IT 50-99-7, Dextrose, biological studies 56-41-7, L-Alanine, biological studies 56-45-1, L-Serine, biological studies 56-81-5, Glycerol, biological studies 71-00-1, L-Histidine, biological studies 77-92-9, Citric acid, biological studies 338-69-2, D-Alanine 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 14808-79-8, Sulfate, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or glutamine synthetase)

L6 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 DUPLICATE 4

AN 2003:127824 BIOSIS <<LOGINID::20080329>>

DN PREV200300127824

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.

AU Chen, Jeffrey M.; ***Alexander, David C.*** ; Behr, Marcel A.; Liu, Jun [Reprint Author]

CS Department of Medical Genetics and Microbiology, University of Toronto, 1 King's College Circle, 4382 Medical Sciences Building, Toronto, ON, M5S 1A8, Canada
jun.liu@utoronto.ca

SO Infection and Immunity, (February 2003) Vol. 71, No. 2, pp. 708-716.
print.
ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-alanine dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG*** -Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine within the host.

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.

AU Chen, Jeffrey M.; ***Alexander, David C.*** ; Behr, Marcel A.; Liu, Jun [Reprint Author]

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IT . . .

```

        disease
        Tuberculosis, Pulmonary (MeSH)
IT  Diseases
    tuberculosis: bacterial disease
    Tuberculosis (MeSH)
IT  Chemicals & Biochemicals
    D-alanine; L-alanine; L-alanine dehydrogenase; L-serine; Mycobacterium
    bovis ***BCG*** vaccines: immunologic-drug, immunostimulant-drug;
    glutamine synthetase [EC 6.3.1.2]

=> s BCG and (alanine dehydrogenase)
L7      33 BCG AND (ALANINE DEHYDROGENASE)

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8      13 DUP REM L7 (20 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L8      ANSWER 1 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
        DUPLICATE 1
AN      2006:636896 BIOSIS <<LOGINID::20080329>>
DN      PREV200600639889
TI      Contribution of L- ***alanine*** ***dehydrogenase*** to in vivo
        persistence and protective efficacy of the ***BCG*** vaccine.
AU      Scandurra, Gabriella M.; Ryan, Anthony A.; Pinto, Rachel; Britton, Warwick
        J.; Triccas, James A. [Reprint Author]
CS      Univ Sydney, Discipline Infect Dis and Immunol, Sydney, NSW 2006,
        Australia
        jamiet@infdis.usyd.edu.au
SO      Microbiology and Immunology, (2006) Vol. 50, No. 10, pp. 805-810.
        CODEN: MIIMDV. ISSN: 0385-5600.
DT      Article
LA      English
ED      Entered STN: 22 Nov 2006
        Last Updated on STN: 22 Nov 2006
AB      The tuberculosis (TB) vaccine strain Mycobacterium bovis ***BCG*** is
        unable to utilise alanine and this deficiency is thought to inhibit the
        growth of the vaccine in vivo and limit vaccine efficacy. In this report
        we demonstrate that L-alanine catabolism can be conferred on ***BCG***
        by introduction of the gene encoding L- ***alanine***
        ***dehydrogenase*** (Ald) of Mycobacterium tuberculosis. Restoration
of      of
        Ald activity did not change the in vivo growth of ***BCG*** in
        macrophages or mice, and protection against aerosol M. tuberculosis
        infection was not altered by addition of ald to the ***BCG*** vaccine.
        These results demonstrate that the inability to utilise L-alanine is not a
        contributing factor to the attenuated phenotype of ***BCG*** and does
        not influence the protective efficacy of the vaccine against TB.
TI      Contribution of L- ***alanine*** ***dehydrogenase*** to in vivo
        persistence and protective efficacy of the ***BCG*** vaccine.
AB      The tuberculosis (TB) vaccine strain Mycobacterium bovis ***BCG*** is
        unable to utilise alanine and this deficiency is thought to inhibit the
        growth of the vaccine in vivo and limit vaccine efficacy. In this report
        we demonstrate that L-alanine catabolism can be conferred on ***BCG***

```


by introduction of the gene encoding L- ***alanine***
 dehydrogenase (Ald) of Mycobacterium tuberculosis. Restoration
 of Ald activity did not change the in vivo growth of ***BCG*** in
 macrophages or mice, and protection against aerosol M. tuberculosis
 infection was not altered by addition of ald to the ***BCG*** vaccine.
 These results demonstrate that the inability to utilise L-alanine is not a
 contributing factor to the attenuated phenotype of ***BCG*** and does
 not influence the protective efficacy of the vaccine against TB.

IT
 blood and lymphatics

IT Diseases
 tuberculosis: bacterial disease, infectious disease, etiology,
 prevention and control
 Tuberculosis (MeSH)

IT Chemicals & Biochemicals
 alanine; L- ***alanine*** ***dehydrogenase*** ; CBG vaccine:
 immunologic-drug, efficacy

RN 302-72-7 (alanine)
 9029-06-5 (L- ***alanine*** ***dehydrogenase***)

GEN Mycobacterium tuberculosis ald gene [Mycobacterium tuberculosis L-
 alanine ***dehydrogenase*** gene] (Mycobacteriaceae)

L8 ANSWER 2 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 DUPLICATE 2

AN 2005:176271 BIOSIS <<LOGINID::20080329>>

DN PREV200500173985

TI Bacterial luciferase is naturally destabilized in Mycobacterium
 tuberculosis and can be used to monitor changes in gene expression.

AU Roberts, Esteban A.; Clark, Amanda; Friedman, Richard L. [Reprint Author]

CS Dept Microbiol and Immunol, Univ Arizona, 1501 N Campbell Ave, Tucson, AZ,
 85724, USA
 rfriedma@email.arizona.edu

SO FEMS Microbiology Letters, (February 1 2005) Vol. 243, No. 1, pp. 243-249.
 print.
 CODEN: FMLED7. ISSN: 0378-1097.

DT Article

LA English

ED Entered STN: 4 May 2005
 Last Updated on STN: 4 May 2005

AB Reporter systems efficient at monitoring temporal gene expression in
 slow-growing mycobacteria would significantly aid the characterization of
 gene expression in specific environments. Bacterial luciferase is a
 reporter that has not been widely used to study gene expression in
 mycobacteria. This report describes the determination of the degradation
 of bacterial luciferase in Mycobacterium tuberculosis H37Ra and its
 utility as a reporter of temporal gene expression in this slow-growing
 mycobacterium. The inducible/ repressible ***alanine***
 dehydrogenase promoter of M. tuberculosis H37Rv was used to track
 the decay kinetics of Vibrio harveyi luciferase in both mid-log phase and
 stationary phase grown M. tuberculosis H37Ra, which proved to be highly
 similar during both phases of growth. The luciferase reporter was then
 used to detect changes in expression from the heat-shock promoter, phsp60,
 of M. bovis ***BCG*** during M. tuberculosis H37Ra growth in culture.
 Quantitative real-time PCR analysis of groEL2, the hsp60 homologue in M.
 tuberculosis, displayed a similar pattern of expression to phsp60-driven
 luciferase. These results strongly suggest that the luciferase reporter

can be used to monitor temporal changes in gene expression in *M. tuberculosis* and may serve as a novel system to examine gene expression under specific conditions. Copyright 2004 Federation of European Microbiological Societies. Published by Elsevier B.V. All rights reserved.

AB. . . *Mycobacterium tuberculosis* H37Ra and its utility as a reporter of temporal gene expression in this slow-growing mycobacterium. The inducible/ repressible ***alanine*** ***dehydrogenase*** promoter of *M. tuberculosis* H37Rv was used to track the decay kinetics of *Vibrio harveyi* luciferase in both mid-log phase. . . growth. The luciferase reporter was then used to detect changes in expression from the heat-shock promoter, *phsp60*, of *M. bovis* ***BCG*** during *M. tuberculosis* H37Ra growth in culture. Quantitative real-time PCR analysis of *groEL2*, the *hsp60* homologue in *M. tuberculosis*, displayed. . .

IT Major Concepts

Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Chemicals & Biochemicals

inducible/repressible ***alanine*** ***dehydrogenase***
promoter; luciferase

L8 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:338335 BIOSIS <<LOGINID::20080329>>
DN PREV200700326336

TI *Mycobacterium bovis* ***BCG*** vaccines exhibit dysregulation of glutamine synthetase in response to nitrogen availability.

AU Chen, J. M. [Reprint Author]; Alexander, D. C.; Behr, M. A.; Liu, J.
CS Univ Toronto, Toronto, ON, Canada

SO Abstracts of the General Meeting of the American Society for Microbiology, (2004) Vol. 104, pp. 639-640.
Meeting Info.: 104th General Meeting of the American-Society-for-Microbiology. New Orleans, LA, USA. May 23 -27, 2004. Amer Soc Microbiol. ISSN: 1060-2011.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 30 May 2007
Last Updated on STN: 30 May 2007

TI *Mycobacterium bovis* ***BCG*** vaccines exhibit dysregulation of glutamine synthetase in response to nitrogen availability.

ORGN . . .
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
Bacteria; Microorganisms

Organism Name

Mycobacterium smegmatis (species)

Mycobacterium marinum (species)

Mycobacterium tuberculosis (species)

Mycobacterium bovis (species): pathogen, strain- ***BCG***

Taxa Notes

Bacteria, Eubacteria, Microorganisms

GEN *Mycobacterium bovis* *ald* gene [*Mycobacterium bovis* ***alanine***
dehydrogenase gene gene] (Mycobacteriaceae); *Mycobacterium bovis*
sdaA gene [*Mycobacterium bovis* serine deaminase gene gene]
(Mycobacteriaceae); *Mycobacterium bovis* *glnA1* gene [*Mycobacterium bovis*.
. . .

L8 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:855955 CAPLUS <<LOGINID::20080329>>

DN 139:363579
 TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing ***alanine*** ***dehydrogenase*** ,
 serine dehydratase and/or glutamine synthetase
 IN Liu, Jun; Chen, Jeffrey; Alexander, David
 PA Can.
 SO PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003089462	A2	20031030	WO 2003-CA566	20030416
	WO 2003089462	A3	20040521		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2481108	A1	20031030	CA 2003-2481108	20030416
	AU 2003218838	A1	20031103	AU 2003-218838	20030416
	GB 2403477	A	20050105	GB 2004-25165	20030416
	GB 2403477	B	20060823		
	CN 1703513	A	20051130	CN 2003-802276	20030416
	JP 2006508633	T	20060316	JP 2003-586182	20030416
	ZA 2004008344	A	20050907	ZA 2004-8344	20041014
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PRAI	US 2002-372450P	P	20020416		
	WO 2003-CA566	W	20030416		

AB The invention relates to a live recombinant Mycobacterium bovis-
 BCG strain comprising a nucleic acid capable of expression, the
 nucleic acid encoding at least one protein or polypeptide that exhibits
 alanine ***dehydrogenase*** activity, glutamine synthetase
 activity, or serine dehydratase activity. The recombinant ***alanine***
 dehydrogenase , serine dehydratase and glutamine synthetase are
 derived from Mycobacterium tuberculosis.

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing ***alanine*** ***dehydrogenase*** ,
 serine dehydratase and/or glutamine synthetase

AB The invention relates to a live recombinant Mycobacterium bovis-
 BCG strain comprising a nucleic acid capable of expression, the
 nucleic acid encoding at least one protein or polypeptide that exhibits
 alanine ***dehydrogenase*** activity, glutamine synthetase
 activity, or serine dehydratase activity. The recombinant ***alanine***
 dehydrogenase , serine dehydratase and glutamine synthetase are
 derived from Mycobacterium tuberculosis.

ST recombinant Mycobacterium bovis ***BCG*** strain tuberculosis vaccine;
 alanine ***dehydrogenase*** serine dehydratase glutamine
 synthetase ***BCG*** tuberculosis vaccine

IT Immunostimulants
 (adjuvants; tuberculosis vaccines including recombinant Mycobacterium

bovis- ***BCG*** strains expressing ***alanine***
 dehydrogenase , serine dehydratase and/or glutamine synthetase)

IT Drug delivery systems
 (carriers; tuberculosis vaccines including recombinant Mycobacterium
 bovis- ***BCG*** strains expressing ***alanine***
 dehydrogenase , serine dehydratase and/or glutamine synthetase)

IT Proteins
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (recombinant; tuberculosis vaccines including recombinant Mycobacterium
 bovis- ***BCG*** strains expressing ***alanine***
 dehydrogenase , serine dehydratase and/or glutamine synthetase)

IT Antitumor agents
 Bladder, neoplasm
 Bos taurus
 Culture media
 DNA sequences
 Human
 Mammalia
 Molecular cloning
 Mycobacterium
 Mycobacterium ***BCG***
 Mycobacterium tuberculosis
 Pathogen
 Protein sequences
 Test kits
 Tuberculosis
 Vaccines
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing ***alanine*** ***dehydrogenase***
 , serine dehydratase and/or glutamine synthetase)

IT Gene, microbial
 Nucleic acids
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis-
 BCG strains expressing ***alanine*** ***dehydrogenase***
 , serine dehydratase and/or glutamine synthetase)

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 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
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 BCG strains expressing ***alanine*** ***dehydrogenase***
 , serine dehydratase and/or glutamine synthetase)

IT 619345-18-5P 619345-20-9P 619345-21-0P 619345-22-1P 619345-23-2P
 619345-24-3P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (amino acid sequence; tuberculosis vaccines including recombinant
 Mycobacterium bovis- ***BCG*** strains expressing ***alanine***
 dehydrogenase , serine dehydratase and/or glutamine synthetase)

IT 619345-19-6
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)

(amino acid sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

IT 619345-25-4P 619345-27-6P 619345-28-7P 619345-29-8P 619345-30-1P 619345-31-2P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nucleotide sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

IT 619345-26-5, DNA (Mycobacterium bovis gene ald)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(nucleotide sequence; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

IT 7440-44-0, Carbon, biological studies 7727-37-9, Nitrogen, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(source; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

IT 9014-27-1P, Serine dehydratase 9023-70-5P, Glutamine synthetase 9029-06-5P, ***Alanine*** ***dehydrogenase*** 175380-16-2P, GenBank Z70692 193398-67-3P, GenBank Z97193 196526-70-2P, GenBank U87280 199902-12-0P, GenBank AL008883 202943-88-2P, GenBank AL021428 335511-06-3P, GenBank AE006919 335512-36-2P, GenBank AE007049 335512-60-2P, GenBank AE007073 335513-04-7P, GenBank AE007117

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

IT 50-99-7, Dextrose, biological studies 56-41-7, L-Alanine, biological studies 56-45-1, L-Serine, biological studies 56-81-5, Glycerol, biological studies 71-00-1, L-Histidine, biological studies 77-92-9, Citric acid, biological studies 338-69-2, D-Alanine 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 14808-79-8, Sulfate, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing ***alanine*** ***dehydrogenase*** , serine dehydratase and/or glutamine synthetase)

L8 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 3

AN 2003:127824 BIOSIS <<LOGINID::20080329>>

DN PREV200300127824

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.

AU Chen, Jeffrey M.; Alexander, David C.; Behr, Marcel A.; Liu, Jun [Reprint Author]

CS Department of Medical Genetics and Microbiology, University of Toronto, 1

King's College Circle, 4382 Medical Sciences Building, Toronto, ON, M5S 1A8, Canada
jun.liu@utoronto.ca

SO Infection and Immunity, (February 2003) Vol. 71, No. 2, pp. 708-716.
print.
ISSN: 0019-9567 (ISSN print).

DT Article
LA English
ED Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-***alanine*** ***dehydrogenase*** gene (ald). Some ***BCG*** strains, such as ***BCG*** -Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine within the host.

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-***alanine*** ***dehydrogenase*** gene (ald). Some ***BCG*** strains, such as ***BCG*** -Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine. . .

IT . . .
tuberculosis: bacterial disease, respiratory system disease
Tuberculosis, Pulmonary (MeSH)

IT Diseases
tuberculosis: bacterial disease
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
D-alanine; L-alanine; L- ***alanine*** ***dehydrogenase*** ;
L-serine; Mycobacterium bovis ***BCG*** vaccines: immunologic-drug,

immunostimulant-drug; glutamine synthetase [EC 6.3.1.2]
 RN 338-69-2 (D-alanine)
 56-41-7 (L-alanine)
 9029-06-5 (L- ***alanine*** ***dehydrogenase***)
 56-45-1 (L-serine)
 9023-70-5 (glutamine synthetase)
 9023-70-5 (EC 6.3.1.2)

L8 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:50676 CAPLUS <<LOGINID::20080329>>

DN 134:114829

TI Tuberculosis vaccine and diagnostics based on the Mycobacterium
 tuberculosis esat-6 gene family

IN Andersen, Peter; Skjot, Rikke

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2378763	A1	20010118	CA 2000-2378763	20000713
	AU 2000059664	A	20010130	AU 2000-59664	20000713
	AU 779495	B2	20050127		
	EP 1200466	A2	20020502	EP 2000-945660	20000713
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003510018	T	20030318	JP 2001-509760	20000713
	US 2004013685	A1	20040122	US 2001-872505	20010601
	AU 2002301509	A1	20030306	AU 2002-301509	20021010
	AU 2005201767	A1	20050519	AU 2005-201767	20050427
	AU 2006252186	A2	20070118	AU 2006-252186	20061221
	AU 2006252186	A1	20070118		
PRAI	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	AU 1998-94338	A3	19981008		
	WO 1998-DK438	W	19981008		
	US 1998-246191	B2	19981230		
	AU 2000-59664	A3	20000713		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	W	20000713		
	US 2001-804980	A2	20010313		
	AU 2002-301509	A3	20021010		

AB The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of Mycobacterium tuberculosis.

IT Mycobacterium ***BCG***
Mycobacterium africanum
Mycobacterium bovis
(fusion protein of ESAT-6 from M. tuberculosis and polypeptide fragment from)

IT 9002-13-5, Urease 9023-70-5, Glutamine synthetase 9029-06-5, L-
Alanine ***dehydrogenase*** 9054-89-1, Superoxide dismutase
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fusion protein with ESAT-6 from Mycobacterium tuberculosis for vaccination and diagnosis)

L8 ANSWER 7 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4

AN 2000:26849 BIOSIS <<LOGINID::20080329>>

DN PREV2000000026849

TI Properties of the 40 kDa antigen of Mycobacterium tuberculosis, a functional L- ***alanine*** ***dehydrogenase*** .

AU Hutter, Bernd; Singh, Mahavir [Reprint author]

CS GBF (Gesellschaft fuer Biotechnologische Forschung m.b.H)-National Research Center for Biotechnology and Department of Biochemistry, Technical University of Braunschweig, 38124, Braunschweig, Germany

SO Biochemical Journal, (Nov. 1, 1999) Vol. 343, No. 3, pp. 669-672. print. ISSN: 0264-6021.

DT Article

LA English

ED Entered STN: 13 Jan 2000
Last Updated on STN: 31 Dec 2001

AB The 40 kDa antigen of Mycobacterium tuberculosis is the first antigen reported to be present in the pathogenic M. tuberculosis, but not in the vaccine strain Mycobacterium bovis ***BCG*** . It is a functional L- ***alanine*** ***dehydrogenase*** (EC 1.4.1.1) and hence one of the few antigens possessing an enzymic activity. This makes the 40 kDa antigen attractive for potential diagnostic and therapeutic interventions. Recently, we developed a strategy to purify quantities of the recombinant protein in active form, and here we describe the biochemical properties of this enzyme. In the oxidative-deamination reaction, the enzyme showed Km values of 13.8 mM and 0.31 mM for L-alanine and NAD+, respectively, in a random-ordered mechanism. Km,app values in the reductive-amination reaction are 35.4 mM, 1.45 mM and 98.2 muM for ammonium, pyruvate and NADH, respectively. The enzyme is highly specific for all of its substrates in both directions. The pH profile indicates that oxidative deamination virtually may not occur at physiological pH. Hence L-alanine most likely is the product of the reaction catalysed in vivo. The enzyme is heat-stable, losing practically no activity at 60 degreeC for several hours.

TI Properties of the 40 kDa antigen of Mycobacterium tuberculosis, a functional L- ***alanine*** ***dehydrogenase*** .

AB. . . the first antigen reported to be present in the pathogenic M. tuberculosis, but not in the vaccine strain Mycobacterium bovis ***BCG*** . It is a functional L- ***alanine*** ***dehydrogenase*** (EC 1.4.1.1) and hence one of the few antigens possessing an enzymic activity. This makes the 40 kDa antigen attractive. . .

IT Major Concepts

Enzymology (Biochemistry and Molecular Biophysics)
 IT Chemicals & Biochemicals
 Mycobacterium tuberculosis L- ***alanine*** ***dehydrogenase***
 [EC 1.4.1.1]: 40 kDa antigen

L8 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1998:684968 CAPLUS <<LOGINID::20080329>>
 DN 129:300060
 TI Novel antigens of Mycobacterium tuberculosis culture filtrates and the
 genes encoding and their diagnostic and prophylactic use
 IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin;
 Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter
 PA Statens Serum Institut, Den.
 SO PCT Int. Appl., 264 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	A1	19981008	CA 1998-2285625	19980401
	AU 9868204	A	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	EP 1449922	B1	20070815		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	AT 370236	T	20070915	AT 2004-76605	19980401
	ES 2291810	T3	20080301	ES 2004-76605	19980401
	CA 2319380	A1	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008

AU 750173	B2	20020711	AU 1998-94338	19981008
EP 1484405	A1	20041208	EP 2004-77071	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AU 2002301509	A1	20030306	AU 2002-301509	20021010
AU 2006252186	A2	20070118	AU 2006-252186	20061221
AU 2006252186	A1	20070118		
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
EP 1998-913536	A3	19980401		
WO 1998-DK132	W	19980401		
AU 1998-94338	A3	19981008		
EP 1998-947412	A3	19981008		
WO 1998-DK438	W	19981008		
AU 2002-301509	A3	20021010		

AB Culture filtrate antigens of Mycobacterium tuberculosis are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a .lambda.gt11 expression vector with monoclonal antibodies. Manuf. of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Escherichia
Mycobacterium
Mycobacterium ***BCG***
Pseudomonas
Salmonella
(expression host for Mycobacterium tuberculosis antigen genes; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium ***BCG*** strain Tokyo ribosome)
208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7
208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9
208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6
208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9
208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4
214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3
214349-26-5 214349-38-9

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, Glutamine synthetase, fusion products 9029-06-5D, ***Alanine*** ***dehydrogenase*** , fusion products 9054-89-1D, Superoxide dismutase, fusion products

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antigen of Mycobacterium tuberculosis; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

L8 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1998:527438 CAPLUS <<LOGINID::20080329>>

DN 129:159059

TI L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as an antigen for use in tuberculosis vaccines

IN Flohe, Leopold; Singh, Mahavir; Hutter, Bernd; Kolk, Arend

PA Germany

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832862	A2	19980730	WO 1998-EP484	19980129
	WO 9832862	A3	19981112		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9860979	A	19980818	AU 1998-60979	19980129
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PRAI EP 1997-101339	A	19970129
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WO 1998-EP484	W	19980129
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AB An antigen of Mycobacterium marinum that may be useful as an antigen in tuberculosis vaccines is described. The antigen is an L- ***alanine*** ***dehydrogenase*** (I). Monoclonal antibodies to the protein react with Mycobacterium tuberculosis but not with Mycobacterium ***BCG***. I is relatively uncommon in bacterial systems and was found at high levels in only a few species of Mycobacterium including M. marinum and M. tuberculosis. Mycobacterium ***BCG*** had a very low I activity. All species of the M. tuberculosis complex carried copies of the dehydrogenase gene regardless of their endogenous I levels. ***Alanine*** ***dehydrogenase*** activity in slow-growing Mycobacteria appeared to correlate with virulence.

TI L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as an antigen for use in tuberculosis vaccines

AB . . . antigen of Mycobacterium marinum that may be useful as an antigen in tuberculosis vaccines is described. The antigen is an L-

alanine ***dehydrogenase*** (I). Monoclonal antibodies to the

protein react with Mycobacterium tuberculosis but not with Mycobacterium ***BCG***. I is relatively uncommon in bacterial systems and was found at high levels in only a few species of Mycobacterium including M. marinum and M. tuberculosis. Mycobacterium ***BCG*** had a very low I activity. All species of the M. tuberculosis complex carried copies of the dehydrogenase gene regardless of their endogenous I levels.

Alanine ***dehydrogenase*** activity in slow-growing Mycobacteria appeared to correlate with virulence.

ST ***alanine*** ***dehydrogenase*** antigen Mycobacterium vaccine tuberculosis

IT Mycobacterium

(***alanine*** ***dehydrogenase*** in; L- ***alanine***

dehydrogenase of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Mycobacterium ***BCG***
 Mycobacterium africanum
 Mycobacterium bovis
 Mycobacterium microti
 (***alanine*** ***dehydrogenase*** of; L- ***alanine***
 dehydrogenase of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Infection
 (bacterial, ***alanine*** ***dehydrogenase*** as antigen in diagnosis of swimmer's disease; L- ***alanine***
 dehydrogenase of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT DNA sequences
 (for ***alanine*** ***dehydrogenase*** of Mycobacterium; L-
 alanine ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Gene, microbial
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
 (for ***alanine*** ***dehydrogenase*** of Mycobacterium, cloning of; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Diagnosis
 (mol., of tuberculosis, with ***alanine*** ***dehydrogenase*** antigen; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Antibodies
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (monoclonal, for antigen of Mycobacterium tuberculosis absent from Mycobacterium ***BCG*** ; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Virulence (microbial)
 (of Mycobacterium, ***alanine*** ***dehydrogenase*** as a marker for; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Protein sequences
 (of ***alanine*** ***dehydrogenase*** of Mycobacterium; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Plasmid vectors
 (pMSK12, gene for antigen of Mycobacterium marinum on; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Vaccines
 (tuberculosis; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Tuberculosis
 (vaccines against, antigen for; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT Mycobacterium marinum
 (L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)
 IT 211176-56-6 211176-58-8

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amino acid sequence; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)

IT 9029-06-5P, L- ***Alanine*** ***dehydrogenase***
 RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
 (as antigen; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)

IT 211176-55-5 211176-57-7 211176-59-9 211176-60-2 211176-61-3
 211176-62-4 211176-64-6 211176-65-7 211176-66-8
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nucleotide sequence; L- ***alanine*** ***dehydrogenase*** of Mycobacterium marinum as antigen for use in tuberculosis vaccines)

L8 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 5

AN 1998:167426 BIOSIS <<LOGINID::20080329>>

DN PREV199800167426

TI Extracellular enzyme activities potentially involved in the pathogenicity of Mycobacterium tuberculosis.

AU Raynaud, Catherine; Etienne, Gilles; Peyron, Pascale; Laneelle, Marie-Antoinette; Daffe, Mamadou [Reprint author]

CS Institut de Pharmacologie et de Biologie Structurale du CNRS, Universite Paul Sabatier, 205 route de Narbonne, 31077 Toulouse Cedex, France

SO Microbiology (Reading), (Feb., 1998) Vol. 144, No. 2, pp. 577-587. print. ISSN: 1350-0872.

DT Article

LA English

ED Entered STN: 6 Apr 1998
 Last Updated on STN: 6 Apr 1998

AB To evaluate the potential contribution of extracellular enzymes to the pathogenicity of mycobacteria, the presence of selected enzyme activities was investigated in the culture filtrates of the obligate human pathogen Mycobacterium tuberculosis, M. bovis ***BCG***, the opportunistic pathogens M. kansasii and M. fortuitum, and the non-pathogenic species M. phlei and M. smegmatis. For M. tuberculosis and M. bovis, 22 enzyme activities were detected in the culture filtrates and/or cell surfaces, of which eight were absent from the culture fluids of non-pathogens: ***alanine*** ***dehydrogenase***, glutamine synthetase, nicotinamidase, isonicotinamidase, superoxide dismutase, catalase, peroxidase and alcohol dehydrogenase. These activities, which correspond to secreted enzymes, formed a significant part (up to 92%) of the total enzyme activities of the bacteria and were absent from the culture fluids and the cell surfaces of the non-pathogenic species M. smegmatis and M. phlei. The extracellular location of superoxide dismutase and glutamine synthetase seemed to be restricted to the obligate pathogens examined. The difference in the enzyme profiles was not attributable to the growth rates of the two groups of bacteria. The presence of the eight enzyme activities in the outermost compartments of obligate pathogens and their absence in those of non-pathogens provides further evidence that these enzymes may be involved in the pathogenicity of mycobacteria. In addition, the eight enzyme activities were demonstrated in the cell extract of M. smegmatis. Stepwise erosion of the cell surface of M.

smegmatis to expose internal capsular constituents showed that the various enzyme activities, with the possible exception of superoxide dismutase, were located more deeply in the cell envelope of this bacterium. This suggests that the molecular architecture of the mycobacterial envelopes may play an important role in the pathogenicity of these organisms.

AB. . . presence of selected enzyme activities was investigated in the culture filtrates of the obligate human pathogen *Mycobacterium tuberculosis*, *M. bovis* ***BCG***, the opportunistic pathogens *M. kansasii* and *M. fortuitum*, and the non-pathogenic species *M. phlei* and *M. smegmatis*. For *M. tuberculosis*. . . were detected in the culture filtrates and/or cell surfaces, of which eight were absent from the culture fluids of non-pathogens: ***alanine*** ***dehydrogenase***, glutamine synthetase, nicotinamidase, isonicotinamidase, superoxide dismutase, catalase, peroxidase and alcohol dehydrogenase. These activities, which correspond to secreted enzymes, formed a. . .

L8 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 6

AN 1995:64955 BIOSIS <<LOGINID::20080329>>

DN PREV199598079255

TI Isolation of a 43 kDa protein from *Mycobacterium tuberculosis* H 3 7Rv and its identification as a pyridine nucleotide transhydrogenase.

AU Deshpande, R. G.; Khan, M. B.; Bhat, D. A.; Navalkar, R. G. [Reprint author]

CS Dep. Microbiol. Immunol., Morehouse Sch. Med., 720 Westview Drive, Atlanta, GA 30310, USA

SO Journal of Applied Bacteriology, (1994) Vol. 77, No. 6, pp. 639-643. CODEN: JABAA4. ISSN: 0021-8847.

DT Article

LA English

ED Entered STN: 8 Feb 1995

Last Updated on STN: 9 Feb 1995

AB A 43 kDa protein (TB43) was isolated from the cell sonicate (CS) of *Mycobacterium tuberculosis* H-37Rv with immobilized metal affinity chromatography (IMAC) on a Ni-nitrilotriacetic acid column. Two-dimensional electrophoresis of the IMAC fraction showed a major spot with an M-r of 43 000 and a pI of approx 6.0. The N-terminal amino acid sequence of TB43 was met-arg-val-gly-ile-pro-asn-glu-thr-lys-asn-asn-glu-phe-arg-val-ala-ile-thr-pro-ala. It showed 86% homology with the N-terminal end of the ***alanine*** ***dehydrogenase*** of *Myco. tuberculosis* and 65% homology with the N-terminal end of the alpha-subunit of the *Escherichia coli* pyridine nucleotide transhydrogenase (Tsh). TB43 did not show any ***alanine*** ***dehydrogenase*** activity and did not react with monoclonal antibody (MAb) HBT10, which is known to recognize the 40 kDa ***alanine*** ***dehydrogenase*** of *Myco. tuberculosis*. It was also not recognized by MAb F29-29 which is known to react with a 43 kDa protein of *Myco. tuberculosis* complex. This protein exhibited strong Tsh activity. A similar 43 kDa protein showing Tsh activity was also isolated by IMAC from *Myco. bovis* CS. However, the pI of the protein was approx 7.0. A similar protein could not be isolated from the CS or culture filtrate of *Myco. bovis* ***BCG*** and *Myco. tuberculosis* H-37Ra. TB43 is a cell-associated pyridine nucleotide transhydrogenase and is distinct from the 40/44 kDa secreted ***alanine*** ***dehydrogenase*** of *Myco. tuberculosis*.

AB. . . 6.0. The N-terminal amino acid sequence of TB43 was met-arg-val-gly-ile-pro-asn-glu-thr-lys-asn-asn-glu-phe-arg-val-ala-ile-thr-pro-ala. It showed 86% homology with the N-terminal end of the

alanine ***dehydrogenase*** of Myco. tuberculosis and 65%
 homology with the N-terminal end of the alpha-subunit of the Escherichia
 coli pyridine nucleotide transhydrogenase (Tsh). TB43 did not show any
 alanine ***dehydrogenase*** activity and did not react with
 monoclonal antibody (MAb) HBT10, which is known to recognize the 40 kDa
 alanine ***dehydrogenase*** of Myco. tuberculosis. It was
 also not recognized by MAb F29-29 which is known to react with a 43 kDa.
 . . protein was apprx 7.0. A similar protein could not be isolated from
 the CS or culture filtrate of Myco. bovis ***BCG*** and Myco.
 tuberculosis H-37Ra. TB43 is a cell-associated pyridine nucleotide
 transhydrogenase and is distinct from the 40/44 kDa secreted
 alanine ***dehydrogenase*** of Myco. tuberculosis.

L8 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
 STN DUPLICATE 7
 AN 1992:391197 BIOSIS <<LOGINID::20080329>>
 DN PREV199294063372; BA94:63372
 TI STRUCTURE AND FUNCTION OF A 40000-MOLECULAR-WEIGHT PROTEIN ANTIGEN OF
 MYCOBACTERIUM-TUBERCULOSIS.
 AU ANDERSEN A B [Reprint author]; ANDERSEN P; LJUNGQVIST L
 CS MYCOBACTERIA DEP, SECTOR BIOTECHNOL, STATENS SERUMINSTITUT, ARTILLERIVEJ
 5, DK 2300 COPENHAGEN S, DENMARK
 SO Infection and Immunity, (1992) Vol. 60, No. 6, pp. 2317-2323.
 CODEN: INFIBR. ISSN: 0019-9567.
 DT Article
 FS BA
 LA ENGLISH
 OS GENBANK-X63069
 ED Entered STN: 24 Aug 1992
 Last Updated on STN: 1 Oct 1992
 AB A gene encoding a protein antigen from Mycobacterium tuberculosis with a
 molecular weight of 40,000 has been sequenced. On the basis of sequence
 homology and functional analyses, we demonstrated that the protein is an
 L- ***alanine*** ***dehydrogenase*** (EC 1.4.1.1.). The enzyme was
 demonstrated in M. tuberculosis and Mycobacterium marinum but not in
 Mycobacterium bovis ***BCG*** . The enzyme may play a role in cell
 wall synthesis because L-alanine is an important constituent of the
 peptidoglycan layer. Although no consensus signal sequence was
 identified, we found evidence which suggests that the enzyme is secreted
 across the cell membrane. The enzyme was characterized and purified by
 chromatography, thus enabling further studies of its role in virulence and
 interaction with the immune system of M. tuberculosis-infected
 individuals.
 AB. . . 40,000 has been sequenced. On the basis of sequence homology and
 functional analyses, we demonstrated that the protein is an L-
 alanine ***dehydrogenase*** (EC 1.4.1.1.). The enzyme was
 demonstrated in M. tuberculosis and Mycobacterium marinum but not in
 Mycobacterium bovis ***BCG*** . The enzyme may play a role in cell
 wall synthesis because L-alanine is an important constituent of the
 peptidoglycan layer.. . .
 IT Sequence Data
 X63069: GENBANK
 IT Miscellaneous Descriptors
 MYCOBACTERIUM-MARINUM L ***ALANINE*** ***DEHYDROGENASE*** EC
 1.4.1.1 CELL WALL SYNTHESIS HOMOLOGY VIRULENCE FACTOR NUCLEOTIDE
 SEQUENCE AMINO ACID SEQUENCE MOLECULAR SEQUENCE DATA GENBANK-X63069
 EMBL-X63069 DDBJ-X63069

RN 384447-46-5 (GENBANK-X63069)
 9029-06-5 (L- ***ALANINE*** ***DEHYDROGENASE***)
 9029-06-5 (EC 1.4.1.1)
 140102-58-5 (GENBANK-X63069)

L8 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1973:54231 CAPLUS <<LOGINID::20080329>>
 DN 78:54231
 OREF 78:8585a,8588a
 TI Amination and transamination processes in cell-free extracts of
 tuberculosis myobacteria
 AU Gorodisskaya, G. Ya.; Karyakina, L. A.; Lazovskaya, A. L.; Uglanova, I. A.
 CS Res. Inst. Epidemiol. Microbiol., Gorki, USSR
 SO Ukrains'kii Biokhimichnii Zhurnal (1946-1977) (1972), 44(5), 653-6
 CODEN: UBZHAZ; ISSN: 0372-3909
 DT Journal
 LA Russian
 AB The alanine and glutamate dehydrogenase as well as aminotransferase
 activities were studied in exts. of 12 mycobacteria strains. The
 cell-free exts. of strains H37Ra, Privalov, Kekin, 2417, Kansas, and Batty
 differed essentially in their levels of ***alanine***
 dehydrogenase activity. Intensive synthesis of alanine was found
 in the Akademia strain (7800 units/mg); the strains E-5, 2417, ***BCG***
 , and Batty showed less of this activity (66-8 units/mg). No
 alanine ***dehydrogenase*** activity was detected in the
 cell-free ext. of strains DT, Vallee, and Vinogradov.
 AB . . . mycobacteria strains. The cell-free exts. of strains H37Ra,
 Privalov, Kekin, 2417, Kansas, and Batty differed essentially in their
 levels of ***alanine*** ***dehydrogenase*** activity. Intensive
 synthesis of alanine was found in the Akademia strain (7800 units/mg); the
 strains E-5, 2417, ***BCG*** , and Batty showed less of this activity
 (66-8 units/mg). No ***alanine*** ***dehydrogenase*** activity
 was detected in the cell-free ext. of strains DT, Vallee, and Vinogradov.
 ST amination process tuberculosis myobacteria; transamination process
 tuberculosis myobacteria; ***alanine*** ***dehydrogenase***
 tuberculosis myobacteria

=> s BCG and (glutamine synthetase)

L9 31 BCG AND (GLUTAMINE SYNTHETASE)

=> dup rem l9

PROCESSING COMPLETED FOR L9

L10 15 DUP REM L9 (16 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:564561 CAPLUS <<LOGINID::20080329>>
 DN 147:8384
 TI Improving antigen delivery and presentation using intracellular bacteria
 by limiting anti-apoptotic bacterial activities in infected cells
 IN Kernodle, Douglas S.
 PA Vanderbilt University, USA; The United States Government as Represented by
 Department of Veteran's Affairs
 SO PCT Int. Appl., 181pp.

CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007059256	A2	20070524	WO 2006-US44429	20061115
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI	US 2005-737525P	P	20051115		
AB	Whole-cell vaccines and methods for increasing the immunogenicity of cellular microorganisms for induction of a protective immune responses in vertebrate hosts are described. Cells used in these vaccines may be used to present antigens foreign to them to induce responses against other infectious agents or cancer cells. The present invention involves an addnl. method of improving antigen presentation by intracellular bacteria in a manner that improves vaccine efficacy. After identifying an enzyme that has an anti-apoptotic effect upon host cells infected by an intracellular microbe, the activity of the enzyme produced by the intracellular microbe is reduced by expressing a mutant copy of the enzyme, thereby modifying the microbe so that it increases immunogenicity. Use of dominant-neg. mutants of the sodA gene for superoxide dismutase of Mycobacterium ***BCG*** to improve immunogenicity is described.				
AB	. . . the microbe so that it increases immunogenicity. Use of dominant-neg. mutants of the sodA gene for superoxide dismutase of Mycobacterium ***BCG*** to improve immunogenicity is described.				
IT	Actinobacillus pleuropneumoniae Bacillus anthracis Brucella Campylobacter Chlamydia pneumoniae Chlamydia trachomatis Chlamydophila psittaci Coxiella burnetii Ehrlichia Ehrlichia ruminantium Escherichia coli Haemophilus Haemophilus ducreyi Haemophilus influenzae Legionella Legionella pneumophila Listeria ivanovii Listeria monocytogenes Mannheimia haemolytica Mycobacterium ***BCG*** Mycobacterium africanum				

Mycobacterium avium
 Mycobacterium avium paratuberculosis
 Mycobacterium intracellulare
 Mycobacterium kansasii
 Mycobacterium marinum
 Mycobacterium tuberculosis
 Mycobacterium ulcerans
 Neisseria gonorrhoeae
 Neisseria meningitidis
 Nocardia
 Nocardia asteroides
 Pasteurella
 Pasteurella multocida
 Pseudomonas
 Pseudomonas aeruginosa
 Rickettsia
 Salmonella
 Salmonella typhi
 Shigella
 Staphylococcus aureus
 Staphylococcus epidermidis
 Streptococcus agalactiae
 Streptococcus pyogenes
 Vibrio cholerae
 Yersinia
 Yersinia enterocolitica
 Yersinia pestis

(improving antigenicity of; improving antigen delivery and presentation using intracellular bacteria by limiting anti-apoptotic bacterial activities in infected cells)

IT Brucella melitensis
 (lumazine synthase of, gene for, expression in Mycobacterium ***BCG*** of; improving antigen delivery and presentation using intracellular bacteria by limiting anti-apoptotic bacterial activities in infected cells)

IT 9023-70-5, ***Glutamine*** ***synthetase*** 9054-89-1,
 Superoxide dismutase
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (dominant-neg. variants of, in improving bacterial immunogenicity; improving antigen delivery and presentation using intracellular bacteria by limiting anti-apoptotic bacterial activities in infected cells)

IT 119799-51-8, Lumazine synthase
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (gene for, of Brucella, expression in Mycobacterium ***BCG*** of; improving antigen delivery and presentation using intracellular bacteria by limiting anti-apoptotic bacterial activities in infected cells)

L10 ANSWER 2 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 AN 2007:422589 BIOSIS <<LOGINID::20080329>>
 DN PREV200700426324
 TI An improved strategy for selective and efficient enrichment of integral plasma membrane proteins of mycobacteria.
 AU Mattow, Jens [Reprint Author]; Siejak, Frank; Hagens, Kristine; Schmidt,

Frank; Koehler, Christian; Treumann, Achim; Schaible, Ulrich E.; Kaufmann, Stefan H. E.

CS Max Planck Inst Infect Biol, Dept Immunol, Schumannstr, 21-22, D-10117 Berlin, Germany
mattow@mpiib-berlin.mpg.de

SO Proteomics, (MAY 2007) Vol. 7, No. 10, pp. 1687-1701.
ISSN: 1615-9853.

DT Article

LA English

ED Entered STN: 8 Aug 2007
Last Updated on STN: 8 Aug 2007

AB Mycobacterial plasma membrane proteins play essential roles in many cellular processes, yet their comprehensive proteomic profiling remains challenging. This is mainly due to obstacles related to their extraction and solubilization. To tackle this problem, we have developed a novel procedure to selectively enrich mycobacterial plasma membrane proteins based on alkaline sodium carbonate washing of crude membranes followed by Triton X-114 phase partitioning. The present study assesses the efficiency of this method by proteome analysis of plasma membrane proteins from *Mycobacterium bovis* ***BCG***. Extracted proteins were separated in parallel by 1-D SDS-PAGE and 2-DE and then analyzed by LC-MS/MS and MALDI-MS/MS. Our study revealed 125 proteins, of which 54 contained 1-14 predicted transmembrane domains (TMD) including nine novel proteins. The 1-D SDS-PAGE-based proteome analysis identified 81 proteins, of which 49 (60.5%) harbored TMD. This approach also revealed many hydrophobic membrane-associated/periplasmic proteins lacking TMD, but only few soluble proteins. The identified proteins were characterized with regard to biological functions and physicochemical properties providing further evidence for the high efficiency of the prefractionation method described herein.

AB. . . partitioning. The present study assesses the efficiency of this method by proteome analysis of plasma membrane proteins from *Mycobacterium bovis* ***BCG***. Extracted proteins were separated in parallel by 1-D SDS-PAGE and 2-DE and then analyzed by LC-MS/MS and MALDI-MS/MS. Our study. . .

IT . . .
Biology); Biochemistry and Molecular Biophysics

IT Parts, Structures, & Systems of Organisms
plasma membrane

IT Chemicals & Biochemicals
Triton X-114; ***glutamine*** ***synthetase*** [EC 6.3.1.2];
plasma membrane protein; enoyl-CoA hydratase [EC 4.2.1.17]; periplasmic
protein; NADH dehydrogenase I; histone-like protein; superoxide
dismutase; UDP-galactopyranose; malate. . .

RN 9002-93-1 (Triton X-114)
9023-70-5 (***glutamine*** ***synthetase***)
9023-70-5 (EC 6.3.1.2)
9027-13-8 (enoyl-CoA hydratase)
9027-13-8 (EC 4.2.1.17)
9054-89-1 (superoxide dismutase)
2956-16-3 (UDP-galactopyranose)
9013-48-3 (malate synthase)
9013-48-3 (EC 4.1.3.2)

. . .

L10 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1

AN 2006:646480 BIOSIS <<LOGINID::20080329>>
 DN PREV200600633287
 TI Protection elicited by two glutamine auxotrophs of Mycobacterium tuberculosis and in vivo growth phenotypes of the four unique ***glutamine*** ***synthetase*** mutants in a murine model.
 AU Lee, Sunhee; Jeon, Bo-Young; Bardarov, Svetoslav; Chen, Mei; Morris, Sheldon L.; Jacobs, William R. Jr. [Reprint Author]
 CS Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA
 jacobsw@hhmi.org
 SO Infection and Immunity, (NOV 2006) Vol. 74, No. 11, pp. 6491-6495.
 CODEN: INFIBR. ISSN: 0019-9567.
 DT Article
 LA English
 ED Entered STN: 22 Nov 2006
 Last Updated on STN: 22 Nov 2006
 AB We generated four individual ***glutamine*** ***synthetase*** (GS) mutants (Delta glnA1, Delta glnA2, Delta glnA3, and Delta glnA4) and one triple mutant (Delta glnA1EA2) of Mycobacterium tuberculosis to investigate the roles of GS enzymes. Subcutaneous immunization with the Delta glnA1EA2 and Delta glnA1 glutamine auxotrophic mutants conferred protection on C57BL/6 mice against an aerosol challenge with virulent M. tuberculosis, which was comparable to that provided by Mycobacterium bovis ***BCG*** vaccination.
 TI Protection elicited by two glutamine auxotrophs of Mycobacterium tuberculosis and in vivo growth phenotypes of the four unique ***glutamine*** ***synthetase*** mutants in a murine model.
 AB We generated four individual ***glutamine*** ***synthetase*** (GS) mutants (Delta glnA1, Delta glnA2, Delta glnA3, and Delta glnA4) and one triple mutant (Delta glnA1EA2) of Mycobacterium tuberculosis. . . on C57BL/6 mice against an aerosol challenge with virulent M. tuberculosis, which was comparable to that provided by Mycobacterium bovis ***BCG*** vaccination.
 IT Major Concepts
 Pharmacology; Enzymology (Biochemistry and Molecular Biophysics)
 IT Chemicals & Biochemicals
 glutamine; ***glutamine*** ***synthetase*** [EC 6.3.1.2];
 BCG vaccine: immunologic-drug, immunostimulant-drug
 RN 6899-04-3 (glutamine)
 9023-70-5 (***glutamine*** ***synthetase***)
 9023-70-5 (EC 6.3.1.2)
 L10 ANSWER 4 OF 15 MEDLINE on STN
 AN 2005150071 MEDLINE <<LOGINID::20080329>>
 DN PubMed ID: 15780437
 TI Protective immunity against Mycobacterium bovis induced by vaccination with Rv3109c--a member of the esat-6 gene family.
 AU Hogarth Philip J; Logan Karen E; Vordermeier H Martin; Singh Mahavir; Hewinson R Glyn; Chambers Mark A
 CS TB Research Group, Veterinary Laboratories Agency Weybridge, New Haw, Addlestone, Surrey KT15 3NB, UK.. p.j.hogarth@vla.defra.gsi.gov.uk
 SO Vaccine, (2005 Apr 8) Vol. 23, No. 20, pp. 2557-64.
 Journal code: 8406899. ISSN: 0264-410X.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LA English

FS Priority Journals
EM 200507
ED Entered STN: 23 Mar 2005
Last Updated on STN: 15 Jul 2005
Entered Medline: 14 Jul 2005

AB In a number of clinical studies the current TB vaccine, Mycobacterium bovis bacille Calmette-Guerin (***BCG***), has provided little or no protection against pulmonary tuberculosis in cattle and man. A new generation of vaccines is therefore required to replace or supplement ***BCG*** . Safety concerns surrounding a number of strategies make protein subunits an attractive approach. Moreover, novel prime-boost strategies based on primary immunisations with ***BCG*** are not only showing promise but also present a clear strategy for testing new TB vaccines in clinical studies. We report the evaluation of six protein vaccine candidates for their ability to induce protective immunity in a murine virulent M. bovis challenge model. One protein (Rv3019c) induced reproducibly significant protection in the spleen and lungs approaching that induced by ***BCG*** . Detailed analysis of antigen-specific T cell responses revealed that despite robust responses in the spleen and lungs of vaccinated mice, there was no correlation between these responses and the protective efficacy of the vaccine. Significantly, Rv3019c also stimulated IFN-gamma responses in PBMC from ***BCG*** vaccinated cattle, indicating its potential for use in a heterologous prime-boost strategy in conjunction with ***BCG*** in the target species.

AB In a number of clinical studies the current TB vaccine, Mycobacterium bovis bacille Calmette-Guerin (***BCG***), has provided little or no protection against pulmonary tuberculosis in cattle and man. A new generation of vaccines is therefore required to replace or supplement ***BCG*** . Safety concerns surrounding a number of strategies make protein subunits an attractive approach. Moreover, novel prime-boost strategies based on primary immunisations with ***BCG*** are not only showing promise but also present a clear strategy for testing new TB vaccines in clinical studies. We. . . M. bovis challenge model. One protein (Rv3019c) induced reproducibly significant protection in the spleen and lungs approaching that induced by ***BCG*** . Detailed analysis of antigen-specific T cell responses revealed that despite robust responses in the spleen and lungs of vaccinated mice,. . . correlation between these responses and the protective efficacy of the vaccine. Significantly, Rv3019c also stimulated IFN-gamma responses in PBMC from ***BCG*** vaccinated cattle, indicating its potential for use in a heterologous prime-boost strategy in conjunction with ***BCG*** in the target species.

CT Check Tags: Female
Animals
*Antigens, Bacterial: GE, genetics
****BCG Vaccine: PD, pharmacology***
Bacterial Proteins
CD4-Positive T-Lymphocytes: IM, immunology
CD8-Positive T-Lymphocytes: IM, immunology
Cell Proliferation
Cell Separation
Cytokines: ME, metabolism

.
. . .
CN 0 (Antigens, Bacterial); 0 (***BCG*** Vaccine); 0 (Bacterial Proteins); 0 (Cytokines); 0 (ESAT-6 protein, Mycobacterium tuberculosis); 0 (Rv3109c vaccine); 0 (Vaccines, Subunit); EC 6.3.1.- (***glutamine*** ***synthetase*** I); EC 6.3.1.2 (Glutamate-Ammonia Ligase)

L10 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 DUPLICATE 2

AN 2004:306182 BIOSIS <<LOGINID::20080329>>

DN PREV200400307494

TI Adenylylation and catalytic properties of Mycobacterium tuberculosis
 glutamine ***synthetase*** expressed in Escherichia coli
 versus mycobacteria.

AU Mehta, Ranjana; Pearson, Josh T.; Mahajan, Sumit; Nath, Abhinav; Hickey,
 Mark J.; Sherman, David R.; Atkins, William M. [Reprint Author]

CS Dept Med Chem, Univ Washington, Seattle, WA, 98195, USA
 winky@u.washington.edu

SO Journal of Biological Chemistry, (May 21 2004) Vol. 279, No. 21, pp.
 22477-22482. print.
 CODEN: JBCHA3. ISSN: 0021-9258.

DT Article

LA English

ED Entered STN: 7 Jul 2004
 Last Updated on STN: 7 Jul 2004

AB Bacterial glutamine synthetases (GSs) are complex dodecameric oligomers
 that play a critical role in nitrogen metabolism, converting ammonia and
 glutamate to glutamine. Recently published reports suggest that GS from
 Mycobacterium tuberculosis (MTb) may be a therapeutic target (Harth, G.,
 and Horwitz, M. A. (2003) Infect. Immun. 71, 456-464). In some
 bacteria, GS is regulated via adenylylation of some or all of the subunits
 within the aggregate; catalytic activity is inversely proportional to the
 extent of adenylylation. The adenylylation and deadenylylation of GS are
 catalyzed by adenylyl transferase (ATase). Here, we demonstrate via
 electrospray ionization mass spectrometry that GS from pathogenic M.
 tuberculosis is adenylylated by the Escherichia coli ATase. The adenylyl
 group can be hydrolyzed by snake venom phosphodiesterase to afford the
 unmodified enzyme. The site of adenylylation of MTb GS by the E. coli
 ATase is Tyr-406, as indicated by the lack of adenylylation of the Y406F
 mutant, and, as expected, is based on amino acid sequence alignments.
 Using electrospray ionization mass spectroscopy methodology, we found that
 GS is not adenylylated when obtained directly from MTb cultures that are
 not supplemented with glutamine. Under these conditions, the highly
 related but non-pathogenic Mycobacterium bovis ***BCG*** yields
 partially (dollar sign25%) adenylylated enzyme. Upon the addition of
 glutamine to the cultures, the MTb GS becomes significantly adenylylated
 (dollar sign30%), whereas the adenylylation of M. bovis ***BCG*** GS
 does not change. Collectively, the results demonstrate that MTb GS is a
 substrate for E. coli ATase, but only low adenylylation states are
 accessible. This parallels the low adenylylation states observed for GS
 from mycobacteria and suggests the intriguing possibility that
 adenylylation in the pathogenic versus non-pathogenic mycobacteria is
 differentially regulated.

TI Adenylylation and catalytic properties of Mycobacterium tuberculosis
 glutamine ***synthetase*** expressed in Escherichia coli
 versus mycobacteria.

AB. . . directly from MTb cultures that are not supplemented with glutamine.
 Under these conditions, the highly related but non-pathogenic
 Mycobacterium bovis ***BCG*** yields partially (dollar sign25%)
 adenylylated enzyme. Upon the addition of glutamine to the cultures, the
 MTb GS becomes significantly adenylylated (dollar sign30%), whereas the
 adenylylation of M. bovis ***BCG*** GS does not change. Collectively,
 the results demonstrate that MTb GS is a substrate for E. coli ATase, but

only. . .

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection;
Metabolism

IT Chemicals & Biochemicals
adenylyl transferase; ammonia; glutamate; glutamine; ***glutamine***
synthetase [EC 6.3.1.2]: catalytic properties, expression;
nitrogen: metabolism

RN 9027-82-1 (adenylyl transferase)
7664-41-7 (ammonia)
11070-68-1 (glutamate)
56-85-9Q (glutamine)
6899-04-3Q (glutamine)
9023-70-5 (***glutamine*** ***synthetase***)
9023-70-5 (EC 6.3.1.2)
7727-37-9 (nitrogen)

L10 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:338335 BIOSIS <<LOGINID::20080329>>
DN PREV200700326336

TI Mycobacterium bovis ***BCG*** vaccines exhibit dysregulation of
glutamine synthetase in response to nitrogen availability.

AU Chen, J. M. [Reprint Author]; Alexander, D. C.; Behr, M. A.; Liu, J.
CS Univ Toronto, Toronto, ON, Canada
SO Abstracts of the General Meeting of the American Society for Microbiology,
(2004) Vol. 104, pp. 639-640.
Meeting Info.: 104th General Meeting of the American-Society-for-
Microbiology. New Orleans, LA, USA. May 23 -27, 2004. Amer Soc Microbiol.
ISSN: 1060-2011.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 30 May 2007
Last Updated on STN: 30 May 2007

TI Mycobacterium bovis ***BCG*** vaccines exhibit dysregulation of
glutamine synthetase in response to nitrogen availability.

IT . . .
(Biochemistry and Molecular Biophysics)

IT Diseases
Mycobacterium infection: bacterial disease, drug therapy

IT Chemicals & Biochemicals
nitrogen; vaccines: immunologic-drug, immunostimulant-drug;
glutamine ***synthetase*** [EC 6.3.1.2]; snake venom
phosphodiesterase

ORGN . . .
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
Bacteria; Microorganisms

Organism Name
Mycobacterium smegmatis (species)
Mycobacterium marinum (species)
Mycobacterium tuberculosis (species)
Mycobacterium bovis (species): pathogen, strain- ***BCG***

Taxa Notes
Bacteria, Eubacteria, Microorganisms

RN 7727-37-9 (nitrogen)
9023-70-5 (***glutamine*** ***synthetase***)
9023-70-5 (EC 6.3.1.2)

9025-82-5 (snake venom phosphodiesterase)

GEN. . . gene gene] (Mycobacteriaceae); Mycobacterium bovis sdaA gene
[Mycobacterium bovis serine deaminase gene gene] (Mycobacteriaceae);
Mycobacterium bovis glnA1 gene [Mycobacterium bovis ***glutamine***
synthetase gene gene] (Mycobacteriaceae); Mycobacterium
tuberculosis glnK gene (Mycobacteriaceae); Mycobacterium tuberculosis gInD
gene (Mycobacteriaceae); Mycobacterium tuberculosis gInE gene
(Mycobacteriaceae)

L10 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:855955 CAPLUS <<LOGINID::20080329>>

DN 139:363579

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine dehydratase
and/or ***glutamine*** ***synthetase***

IN Liu, Jun; Chen, Jeffrey; Alexander, David

PA Can.

SO PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2003089462	A2	20031030	WO 2003-CA566	20030416
	WO 2003089462	A3	20040521		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,				
	PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,				
	TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				
	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				
	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,				
	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2481108	A1	20031030	CA 2003-2481108	20030416
	AU 2003218838	A1	20031103	AU 2003-218838	20030416
	GB 2403477	A	20050105	GB 2004-25165	20030416
	GB 2403477	B	20060823		
	CN 1703513	A	20051130	CN 2003-802276	20030416
	JP 2006508633	T	20060316	JP 2003-586182	20030416
	ZA 2004008344	A	20050907	ZA 2004-8344	20041014
	US 2007264286	A1	20071115	US 2006-511718	20060728
PRAI	US 2002-372450P	P	20020416		
	WO 2003-CA566	W	20030416		

AB The invention relates to a live recombinant Mycobacterium bovis-
BCG strain comprising a nucleic acid capable of expression, the
nucleic acid encoding at least one protein or polypeptide that exhibits
alanine dehydrogenase activity, ***glutamine*** ***synthetase***
activity, or serine dehydratase activity. The recombinant alanine
dehydrogenase, serine dehydratase and ***glutamine***
synthetase are derived from Mycobacterium tuberculosis.

TI Tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine dehydratase
and/or ***glutamine*** ***synthetase***

AB The invention relates to a live recombinant Mycobacterium bovis-

BCG strain comprising a nucleic acid capable of expression, the nucleic acid encoding at least one protein or polypeptide that exhibits alanine dehydrogenase activity, ***glutamine*** ***synthetase*** activity, or serine dehydratase activity. The recombinant alanine dehydrogenase, serine dehydratase and ***glutamine*** ***synthetase*** are derived from Mycobacterium tuberculosis.

ST recombinant Mycobacterium bovis ***BCG*** strain tuberculosis vaccine; alanine dehydrogenase serine dehydratase ***glutamine*** ***synthetase*** ***BCG*** tuberculosis vaccine

IT Immunostimulants
 (adjuvants; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT Drug delivery systems
 (carriers; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT Proteins
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (recombinant; tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT Antitumor agents
 Bladder, neoplasm
 Bos taurus
 Culture media
 DNA sequences
 Human
 Mammalia
 Molecular cloning
 Mycobacterium
 Mycobacterium ***BCG***
 Mycobacterium tuberculosis
 Pathogen
 Protein sequences
 Test kits
 Tuberculosis
 Vaccines
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT Gene, microbial
 Nucleic acids
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT Antigens
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tuberculosis vaccines including recombinant Mycobacterium bovis- ***BCG*** strains expressing alanine dehydrogenase, serine dehydratase and/or ***glutamine*** ***synthetase***)

IT 619345-18-5P 619345-20-9P 619345-21-0P 619345-22-1P 619345-23-2P
619345-24-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(amino acid sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or ***glutamine***
synthetase)

IT 619345-19-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(amino acid sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or ***glutamine***
synthetase)

IT 619345-25-4P 619345-27-6P 619345-28-7P 619345-29-8P 619345-30-1P
619345-31-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(nucleotide sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or ***glutamine***
synthetase)

IT 619345-26-5, DNA (Mycobacterium bovis gene ald)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(nucleotide sequence; tuberculosis vaccines including recombinant
Mycobacterium bovis- ***BCG*** strains expressing alanine
dehydrogenase, serine dehydratase and/or ***glutamine***
synthetase)

IT 7440-44-0, Carbon, biological studies 7727-37-9, Nitrogen, biological
studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(source; tuberculosis vaccines including recombinant Mycobacterium
bovis- ***BCG*** strains expressing alanine dehydrogenase, serine
dehydratase and/or ***glutamine*** ***synthetase***)

IT 9014-27-1P, Serine dehydratase 9023-70-5P, ***Glutamine***
synthetase 9029-06-5P, Alanine dehydrogenase 175380-16-2P,
GenBank Z70692 193398-67-3P, GenBank Z97193 196526-70-2P, GenBank
U87280 199902-12-0P, GenBank AL008883 202943-88-2P, GenBank AL021428
335511-06-3P, GenBank AE006919 335512-36-2P, GenBank AE007049
335512-60-2P, GenBank AE007073 335513-04-7P, GenBank AE007117
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or ***glutamine*** ***synthetase***)

IT 50-99-7, Dextrose, biological studies 56-41-7, L-Alanine, biological
studies 56-45-1, L-Serine, biological studies 56-81-5, Glycerol,
biological studies 71-00-1, L-Histidine, biological studies 77-92-9,
Citric acid, biological studies 338-69-2, D-Alanine 7439-89-6, Iron,
biological studies 7439-95-4, Magnesium, biological studies
14808-79-8, Sulfate, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(tuberculosis vaccines including recombinant Mycobacterium bovis-
BCG strains expressing alanine dehydrogenase, serine
dehydratase and/or ***glutamine*** ***synthetase***)

L10 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 3

AN 2003:127824 BIOSIS <<LOGINID::20080329>>

DN PREV200300127824

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and
serine catabolism.

AU Chen, Jeffrey M.; Alexander, David C.; Behr, Marcel A.; Liu, Jun [Reprint
Author]

CS Department of Medical Genetics and Microbiology, University of Toronto, 1
King's College Circle, 4382 Medical Sciences Building, Toronto, ON, M5S
1A8, Canada
jun.liu@utoronto.ca

SO Infection and Immunity, (February 2003) Vol. 71, No. 2, pp. 708-716.
print.

ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 5 Mar 2003

Last Updated on STN: 5 Mar 2003

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the
prevention of tuberculosis (TB) in humans. ***BCG*** is a live
vaccine, and induction of immunity to TB requires productive infection of
the host by ***BCG***. However, ***BCG*** is not a satisfactory
vaccine, because it fails to protect against pulmonary TB in adults. In
this study, we found that ***BCG*** strains cannot utilize many
naturally occurring amino acids as the sole nitrogen source for growth.
This defect is caused, at least partially, by the lack of functional
metabolic enzymes. All ***BCG*** strains are unable to catabolize
L-alanine or D-alanine due to a frameshift mutation in the L-alanine
dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***
-Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine,
apparently due to inadequate expression of L-serine deaminase (sdaA). We
also found that undegraded alanine and serine inhibit the growth of
BCG through blockage of ***glutamine*** ***synthetase***.
These results suggest that ***BCG*** strains are limited in nitrogen
metabolic capacity and predict defects that may restrict multiplication
and persistence of the live vaccine within the host.

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and
serine catabolism.

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the
prevention of tuberculosis (TB) in humans. ***BCG*** is a live
vaccine, and induction of immunity to TB requires productive infection of
the host by ***BCG***. However, ***BCG*** is not a satisfactory
vaccine, because it fails to protect against pulmonary TB in adults. In
this study, we found that ***BCG*** strains cannot utilize many
naturally occurring amino acids as the sole nitrogen source for growth.
This defect is caused, at least partially, by the lack of functional
metabolic enzymes. All ***BCG*** strains are unable to catabolize
L-alanine or D-alanine due to a frameshift mutation in the L-alanine
dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***
-Pasteur and ***BCG*** -Frappier, cannot catabolize L-serine,

apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of ***glutamine*** ***synthetase***. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine. . .

IT . . .
disease
Tuberculosis, Pulmonary (MeSH)
IT Diseases
tuberculosis: bacterial disease
Tuberculosis (MeSH)
IT Chemicals & Biochemicals
D-alanine; L-alanine; L-alanine dehydrogenase; L-serine; Mycobacterium bovis ***BCG*** vaccines: immunologic-drug, immunostimulant-drug; ***glutamine*** ***synthetase*** [EC 6.3.1.2]
RN 338-69-2 (D-alanine)
56-41-7 (L-alanine)
9029-06-5 (L-alanine dehydrogenase)
56-45-1 (L-serine)
9023-70-5 (***glutamine*** ***synthetase***)
9023-70-5 (EC 6.3.1.2)

L10 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:615357 CAPLUS <<LOGINID::20080329>>
DN 137:184446
TI Attenuated bacteria having reduced anti-apoptotic enzyme activity to enhance immunogenicity and for use as vaccines against infectious diseases
IN Kernodle, Douglas S.; Bochan, Markian R.
PA Vanderbilt University, USA; The United States Government as Represented by the Department of Veteran's Affairs
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002062298	A2	20020815	WO 2002-US3451	20020207
	WO 2002062298	A3	20030220		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2437596	A1	20020815	CA 2002-2437596	20020207
	AU 2002240269	A1	20020819	AU 2002-240269	20020207
	AU 2002240269	B2	20070621		
	EP 1361794	A2	20031119	EP 2002-706163	20020207
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2005504502	T	20050217	JP 2002-562306	20020207
	ZA 2003006058	A	20040602	ZA 2003-6058	20030806

	IN 2003DN01267	A	20050527	IN 2003-DN1267	20030811
	US 2004109875	A1	20040610	US 2004-467644	20040120
PRAI	US 2001-267328P	P	20010207		
	US 2001-322989P	P	20010918		
	WO 2002-US3451	W	20020207		

AB Whole-cell vaccines and methods for their use in producing protective immune responses in vertebrate hosts subsequently exposed to pathogenic bacteria. The present invention involves a method of enhancing antigen presentation by intracellular bacteria in a manner that improves vaccine efficacy. After identifying an enzyme that has an anti-apoptotic effect upon host cells infected by an intracellular microbe, the activity of the enzyme is reduced, thereby modifying the microbe so that it increases immunogenicity. Also, the present invention provides a method of incrementally modifying enzyme activity to produce incrementally attenuated mutants of the microbe from which an effective vaccine candidate can be selected.

IT Actinobacillus pleuropneumoniae
Bacillus anthracis
Brucella
Brucella melitensis
Campylobacter
Chlamydia
Chlamydia pneumoniae
Chlamydia trachomatis
Chlamydophila psittaci
Coxiella burnetii
Ehrlichia
Ehrlichia ruminantium
Escherichia coli
Eubacteria
Haemophilus
Haemophilus ducreyi
Haemophilus influenzae
Human
Immunodeficiency
Immunostimulation
Infection
Legionella
Legionella pneumophila
Listeria ivanovii
Listeria monocytogenes
Mammalia
Mannheimia haemolytica
Mutagenesis
Mycobacterium ***BCG***
Mycobacterium africanum
Mycobacterium avium
Mycobacterium avium paratuberculosis
Mycobacterium bovis
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium marinum
Mycobacterium tuberculosis
Mycobacterium ulcerans
Neisseria gonorrhoeae
Neisseria meningitidis
Nocardia

Nocardia asteroides
 Pasteurella
 Pasteurella multocida
 Pseudomonas
 Pseudomonas aeruginosa
 Respiratory system
 Rickettsia
 Salmonella
 Salmonella typhi
 Shigella
 Staphylococcus aureus
 Staphylococcus epidermidis
 Streptococcus agalactiae
 Streptococcus pyogenes
 Tuberculosis
 Vaccines
 Vibrio cholerae
 Yersinia
 Yersinia enterocolitica
 Yersinia pestis

(attenuated bacteria having reduced anti-apoptotic enzyme activity to
 enhance immunogenicity and for use as vaccines against infectious
 diseases)

IT 9023-70-5, ***Glutamine*** ***synthetase*** 9054-89-1,
 Superoxide dismutase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (attenuated bacteria having reduced anti-apoptotic enzyme activity to
 enhance immunogenicity and for use as vaccines against infectious
 diseases)

L10 ANSWER 10 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
 STN DUPLICATE 4

AN 2002:600488 BIOSIS <<LOGINID::20080329>>

DN PREV200200600488

TI Production of avirulent mutants of Mycobacterium bovis with vaccine
 properties by the use of illegitimate recombination and screening of
 stationary-phase cultures.

AU Collins, D. M. [Reprint author]; Wilson, T.; Campbell, S.; Buddle, B. M.;
 Wards, B. J.; Hotter, G.; De Lisle, G. W.

CS Wallaceville Animal Research Centre, AgResearch, PO Box 40063, Upper Hutt,
 New Zealand
 desmond.collins@agresearch.co.nz

SO Microbiology (Reading), (October, 2002) Vol. 148, No. 10, pp. 3019-3027.
 print.
 ISSN: 1350-0872.

DT Article

LA English

ED Entered STN: 20 Nov 2002

Last Updated on STN: 20 Nov 2002

AB A better tuberculosis vaccine is urgently required to control the
 continuing epidemic. Molecular techniques are now available to produce a
 better live vaccine than ***BCG*** by producing avirulent strains of
 the Mycobacterium tuberculosis complex with known gene deletions. In this
 study, 1000 illegitimate recombinants of Mycobacterium bovis were produced
 by illegitimate recombination with fragments of mycobacterial DNA
 containing a kanamycin resistance gene. Eight recombinant strains were
 selected on the basis of their inability to grow when stationary-phase

cultures were inoculated into minimal medium. Five of these recombinants were found to be avirulent when inoculated into guinea pigs. Two of the avirulent recombinants produced vaccine efficacy comparable to ***BCG*** against an aerosol challenge in guinea pigs with *M. bovis*. One of these recombinants had an inactivated *glnA2* gene encoding a putative ***glutamine*** ***synthetase***. Transcriptional analysis showed that inactivation of *glnA2* did not affect expression of the downstream *glnE* gene. The other recombinant had a block of 12 genes deleted, including the sigma factor gene *sigG*. Two avirulent recombinants with an inactivated *pckA* gene, encoding phosphoenolpyruvate carboxykinase which catalyses the first step of gluconeogenesis, induced poor protection against tuberculosis. It is clear that live avirulent strains of the *M. tuberculosis* complex vary widely in their ability as vaccines to protect against tuberculosis. Improved models may be required to more clearly determine the difference in protective effect between ***BCG*** and potential new tuberculosis vaccines.

AB. . . is urgently required to control the continuing epidemic. Molecular techniques are now available to produce a better live vaccine than ***BCG*** by producing avirulent strains of the *Mycobacterium tuberculosis* complex with known gene deletions. In this study, 1000 illegitimate recombinants of. . . were found to be avirulent when inoculated into guinea pigs. Two of the avirulent recombinants produced vaccine efficacy comparable to ***BCG*** against an aerosol challenge in guinea pigs with *M. bovis*. One of these recombinants had an inactivated *glnA2* gene encoding a putative ***glutamine*** ***synthetase***. Transcriptional analysis showed that inactivation of *glnA2* did not affect expression of the downstream *glnE* gene. The other recombinant had. . . vaccines to protect against tuberculosis. Improved models may be required to more clearly determine the difference in protective effect between ***BCG*** and potential new tuberculosis vaccines.

IT . . . and Molecular Biophysics); Pharmacology

IT Diseases
tuberculosis: bacterial disease
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
Mycobacterium bovis vaccine: immunologic-drug, immunostimulant-drug, vaccine; ***glutamine*** ***synthetase***

RN 9023-70-5 (***glutamine*** ***synthetase***)

L10 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:50676 CAPLUS <<LOGINID::20080329>>

DN 134:114829

TI Tuberculosis vaccine and diagnostics based on the *Mycobacterium tuberculosis* *esat-6* gene family

IN Andersen, Peter; Skjot, Rikke

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2378763	A1	20010118	CA 2000-2378763	20000713
AU 2000059664	A	20010130	AU 2000-59664	20000713
AU 779495	B2	20050127		
EP 1200466	A2	20020502	EP 2000-945660	20000713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510018	T	20030318	JP 2001-509760	20000713
US 2004013685	A1	20040122	US 2001-872505	20010601
AU 2002301509	A1	20030306	AU 2002-301509	20021010
AU 2005201767	A1	20050519	AU 2005-201767	20050427
AU 2006252186	A2	20070118	AU 2006-252186	20061221
AU 2006252186	A1	20070118		
PRAI DK 1999-1020	A	19990713		
US 1999-144011P	P	19990715		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
AU 1998-94338	A3	19981008		
WO 1998-DK438	W	19981008		
US 1998-246191	B2	19981230		
AU 2000-59664	A3	20000713		
US 2000-615947	A2	20000713		
WO 2000-DK398	W	20000713		
US 2001-804980	A2	20010313		
AU 2002-301509	A3	20021010		
AB	The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of Mycobacterium tuberculosis.			
IT	Mycobacterium ***BCG*** Mycobacterium africanum Mycobacterium bovis (fusion protein of ESAT-6 from M. tuberculosis and polypeptide fragment from)			
IT	9002-13-5, Urease 9023-70-5, ***Glutamine*** ***synthetase*** 9029-06-5, L-Alanine dehydrogenase 9054-89-1, Superoxide dismutase RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (fusion protein with ESAT-6 from Mycobacterium tuberculosis for vaccination and diagnosis)			
L10	ANSWER 12 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 5			
AN	2002:138685 BIOSIS <<LOGINID::20080329>>			
DN	PREV200200138685			
TI	Purification and characterization of extracellular and intracellular glutamine synthetases from Mycobacterium bovis ***BCG*** .			
AU	Suh, Chang-Il; Lim, Jun-Man; Sung, Ha-Chin [Reprint author]			
CS	Graduate School of Biotechnology, Korea University, Seoul, 136-701, South Korea hcsung@mail.korea.ac.kr			

SO Journal of Microbiology and Biotechnology, (December, 2001) Vol. 11, No. 6, pp. 946-950. print.
ISSN: 1017-7825.

DT Article

LA English

ED Entered STN: 6 Feb 2002
Last Updated on STN: 26 Feb 2002

AB Slow-growing pathogenic mycobacterium species, including *Mycobacterium bovis* ***BCG***, secrete a large amount of ***glutamine*** ***synthetase*** into culture media. Extracellular and intracellular glutamine synthetases were purified from *M. bovis* ***BCG***. While the native molecular weights of both glutamine synthetases were estimated to be 370.2 kDa, those of the subunits were 61.7 kDa, indicating that the native forms were composed of 6 subunits. The enzymes showed a high thermal stability and high degree of sequence similarity with the ***glutamine*** ***synthetase*** from *M. tuberculosis* in the N-terminal amino acid sequence. Western blotting analysis indicated that the antibodies prepared against both the extracellular and intracellular enzymes exhibited common antigen determinants.

TI Purification and characterization of extracellular and intracellular glutamine synthetases from *Mycobacterium bovis* ***BCG***.

AB Slow-growing pathogenic mycobacterium species, including *Mycobacterium bovis* ***BCG***, secrete a large amount of ***glutamine*** ***synthetase*** into culture media. Extracellular and intracellular glutamine synthetases were purified from *M. bovis* ***BCG***. While the native molecular weights of both glutamine synthetases were estimated to be 370.2 kDa, those of the subunits were. . . were composed of 6 subunits. The enzymes showed a high thermal stability and high degree of sequence similarity with the ***glutamine*** ***synthetase*** from *M. tuberculosis* in the N-terminal amino acid sequence. Western blotting analysis indicated that the antibodies prepared against both the. . .

ORGN . . .
Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
Bacteria; Microorganisms
Organism Name
BCG
Mycobacterium bovis: strain- ***BCG***
mycobacteria: pathogen, slow-growing
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L10 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1998:684968 CAPLUS <<LOGINID::20080329>>

DN 129:300060

TI Novel antigens of *Mycobacterium tuberculosis* culture filtrates and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	A1	19981008	CA 1998-2285625	19980401
	AU 9868204	A	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	EP 1449922	B1	20070815		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	AT 370236	T	20070915	AT 2004-76605	19980401
	ES 2291810	T3	20080301	ES 2004-76605	19980401
	CA 2319380	A1	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	AU 2002301509	A1	20030306	AU 2002-301509	20021010
	AU 2006252186	A2	20070118	AU 2006-252186	20061221
	AU 2006252186	A1	20070118		
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		
	WO 1998-DK132	W	19980401		
	AU 1998-94338	A3	19981008		
	EP 1998-947412	A3	19981008		
	WO 1998-DK438	W	19981008		
	AU 2002-301509	A3	20021010		

AB Culture filtrate antigens of Mycobacterium tuberculosis are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a .lambda.gt11 expression vector with monoclonal antibodies. Manuf. of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Escherichia
Mycobacterium
Mycobacterium ***BCG***
Pseudomonas
Salmonella

(expression host for Mycobacterium tuberculosis antigen genes; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium ***BCG*** strain Tokyo ribosome)
208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7
208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9
208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6
208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9
208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4
214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3
214349-26-5 214349-38-9

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, ***Glutamine***
synthetase, fusion products 9029-06-5D, Alanine dehydrogenase,
fusion products 9054-89-1D, Superoxide dismutase, fusion products
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antigen of Mycobacterium tuberculosis; novel antigens of Mycobacterium tuberculosis culture filtrates and genes encoding and their diagnostic and prophylactic use)

L10 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1998:621228 CAPLUS <<LOGINID::20080329>>

DN 129:240866

TI Positive-selection cloning vectors using a resistance marker containing an intein sequence to identify open reading frames

IN Jacobs, William R.; Daugelat, Sabine

PA Albert Einstein College of Medicine of Yeshiva University, USA

SO PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840394	A1	19980917	WO 1998-US4805	19980310
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5981182	A	19991109	US 1997-816721	19970313
AU 9869389	A	19980929	AU 1998-69389	19980310
PRAI US 1997-816721	A	19970313		
WO 1998-US4805	W	19980310		

AB Cloning vectors that make use of the self-excising properties of inteins to identify open reading frames are described. An intein is excised from a larger protein providing certain minimal sequence requirements around the excision sites are met. The remainder of the intein may include a foreign protein. If the intein is introduced into a resistance marker, then successful self-excision will lead to the development of resistance. If a sequence that is not an open reading frame is cloned into the intein sequence, then the resistance marker product will not be formed and the organism carrying the sequence will be sensitive to the selective agent. The vectors include a cloning site in the intein coding region, and appropriate promoters and replication origins. The vector constructs of the present invention may contain DNA of interest cloned into a unique restriction site of the intein, and may be used as a vaccine alone or transformed into a vaccine vector. In particular, these vectors are intended for use in the cloning of sequences encoding protective antigens. The use of the intein of the Mycobacterium tuberculosis recA gene in the aph (kanamycin resistance gene) is demonstrated using Escherichia coli and Mycobacterium smegmatis as hosts. When the intein can be correctly spliced, a very large fraction (>75%) of cfu's are kanamycin resistant. In constructs designed to prevent excision of the intein, the frequency of kanamycin resistant cfu's fell to as low as 1 in 4.times.10⁶ in E. coli and 1 in 3.times.10⁸ in M. smegmatis. Further anal. showed that splicing efficiency was very dependent upon the site used for integration of the foreign sequence. Use of the method to clone open reading frames from well characterized genomes (mycobacteriophage L5, Haemophilus influenzae) is demonstrated.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Mycobacterium ***BCG***
Mycobacterium microti
Mycobacterium tuberculosis
(intein of recA gene of; pos.-selection cloning vectors using resistance marker contg. intein sequence to identify open reading frames)

IT 9002-03-3D, Dihydrofolate reductase, intein-contg. precursors
9002-06-6D, Thymidine kinase, intein-contg. precursors 9012-49-1D,
Aspartate transcarbamylase, intein-contg. precursors 9014-52-2D,
Tryptophan synthetase, intein-contg. precursors 9016-12-0D,
Hypoxanthine-guanine phosphoribosyltransferase, intein-contg. precursors
9023-69-2D, Asparagine synthetase, intein-contg. precursors 9023-70-5D,
Glutamine ***synthetase***, intein-contg. precursors
9024-60-6D, Ornithine decarboxylase, intein-contg. precursors
9024-93-5D, Dihydroorotase, intein-contg. precursors 9026-93-1D,
Adenosine deaminase, intein-contg. precursors 9027-80-9D, Adenine
phosphoribosyltransferase, intein-contg. precursors 9028-27-7D,
Histidinol dehydrogenase, intein-contg. precursors 37233-48-0D, Carbamyl

phosphate synthase, intein-contg. precursors 37350-22-4D,
Xanthine-guanine phosphoribosyltransferase, intein-contg. precursors
56941-28-7D, Aminoglycoside phosphotransferase, intein-contg. precursors
88361-67-5D, Hygromycin B phosphotransferase, intein-contg. precursors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)

(in selection of antibiotic resistant clones; pos.-selection cloning
vectors using resistance marker contg. intein sequence to identify open
reading frames)

L10 ANSWER 15 OF 15 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 6
AN 1998:167426 BIOSIS <<LOGINID::20080329>>
DN PREV199800167426
TI Extracellular enzyme activities potentially involved in the pathogenicity
of Mycobacterium tuberculosis.
AU Raynaud, Catherine; Etienne, Gilles; Peyron, Pascale; Laneelle,
Marie-Antoinette; Daffe, Mamadou [Reprint author]
CS Institut de Pharmacologie et de Biologie Structurale du CNRS, Universite
Paul Sabatier, 205 route de Narbonne, 31077 Toulouse Cedex, France
SO Microbiology (Reading), (Feb., 1998) Vol. 144, No. 2, pp. 577-587. print.
ISSN: 1350-0872.
DT Article
LA English
ED Entered STN: 6 Apr 1998
Last Updated on STN: 6 Apr 1998
AB To evaluate the potential contribution of extracellular enzymes to the
pathogenicity of mycobacteria, the presence of selected enzyme activities
was investigated in the culture filtrates of the obligate human pathogen
Mycobacterium tuberculosis, M. bovis ***BCG***, the opportunistic
pathogens M. kansasii and M. fortuitum, and the non-pathogenic species M.
phlei and M. smegmatis. For M. tuberculosis and M. bovis, 22 enzyme
activities were detected in the culture filtrates and/or cell surfaces, of
which eight were absent from the culture fluids of non-pathogens: alanine
dehydrogenase, ***glutamine*** ***synthetase***, nicotinamidase,
isonicotinamidase, superoxide dismutase, catalase, peroxidase and alcohol
dehydrogenase. These activities, which correspond to secreted enzymes,
formed a significant part (up to 92%) of the total enzyme activities of
the bacteria and were absent from the culture fluids and the cell surfaces
of the non-pathogenic species M. smegmatis and M. phlei. The
extracellular location of superoxide dismutase and ***glutamine***
synthetase seemed to be restricted to the obligate pathogens
examined. The difference in the enzyme profiles was not attributable to
the growth rates of the two groups of bacteria. The presence of the eight
enzyme activities in the outermost compartments of obligate pathogens and
their absence in those of non-pathogens provides further evidence that
these enzymes may be involved in the pathogenicity of mycobacteria. In
addition, the eight enzyme activities were demonstrated in the cell
extract of M. smegmatis. Stepwise erosion of the cell surface of M.
smegmatis to expose internal capsular constituents showed that the various
enzyme activities, with the possible exception of superoxide dismutase,
were located more deeply in the cell envelope of this bacterium. This
suggests that the molecular architecture of the mycobacterial envelopes
may play an important role in the pathogenicity of these organisms.
AB. . . presence of selected enzyme activities was investigated in the
culture filtrates of the obligate human pathogen Mycobacterium
tuberculosis, M. bovis ***BCG***, the opportunistic pathogens M.

kansasii and M. fortuitum, and the non-pathogenic species M. phlei and M. smegmatis. For M. tuberculosis. . . in the culture filtrates and/or cell surfaces, of which eight were absent from the culture fluids of non-pathogens: alanine dehydrogenase, ***glutamine***
 synthetase, nicotinamidase, isonicotinamidase, superoxide dismutase, catalase, peroxidase and alcohol dehydrogenase. These activities, which correspond to secreted enzymes, formed a significant part. . . and the cell surfaces of the non-pathogenic species M. smegmatis and M. phlei. The extracellular location of superoxide dismutase and ***glutamine*** ***synthetase*** seemed to be restricted to the obligate pathogens examined. The difference in the enzyme profiles was not attributable to the. . .

IT Major Concepts
 Bacteriology; Enzymology (Biochemistry and Molecular Biophysics);
 Infection
 IT Diseases
 tuberculosis: bacterial disease
 Tuberculosis (MeSH)
 IT Chemicals & Biochemicals
 glutamine ***synthetase***; superoxide dismutase
 RN 9023-70-5 (***glutamine*** ***synthetase***)
 9054-89-1 (superoxide dismutase)

=> s BCG and (L-serine dehydratase)
 L11 1 BCG AND (L-SERINE DEHYDRATASE)

=> d bib ab kwic

L11 ANSWER 1 OF 1 MEDLINE on STN
 AN 2003033719 MEDLINE <<LOGINID::20080329>>
 DN PubMed ID: 12540549
 TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.
 AU Chen Jeffrey M; Alexander David C; Behr Marcel A; Liu Jun
 CS Department of Medical Genetics and Microbiology, University of Toronto, Ontario M5S 1A8, Canada.
 SO Infection and immunity, (2003 Feb) Vol. 71, No. 2, pp. 708-16.
 Journal code: 0246127. ISSN: 0019-9567.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LA English
 FS Priority Journals
 OS GENBANK-AF531175; GENBANK-AF531176; GENBANK-AF531177
 EM 200302
 ED Entered STN: 24 Jan 2003
 Last Updated on STN: 27 Feb 2003
 Entered Medline: 26 Feb 2003
 AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional

metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-alanine dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***-Pasteur and ***BCG***-Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine within the host.

TI Mycobacterium bovis ***BCG*** vaccines exhibit defects in alanine and serine catabolism.

AB Mycobacterium bovis ***BCG*** is the only accepted vaccine for the prevention of tuberculosis (TB) in humans. ***BCG*** is a live vaccine, and induction of immunity to TB requires productive infection of the host by ***BCG***. However, ***BCG*** is not a satisfactory vaccine, because it fails to protect against pulmonary TB in adults. In this study, we found that ***BCG*** strains cannot utilize many naturally occurring amino acids as the sole nitrogen source for growth. This defect is caused, at least partially, by the lack of functional metabolic enzymes. All ***BCG*** strains are unable to catabolize L-alanine or D-alanine due to a frameshift mutation in the L-alanine dehydrogenase gene (ald). Some ***BCG*** strains, such as ***BCG***-Pasteur and ***BCG***-Frappier, cannot catabolize L-serine, apparently due to inadequate expression of L-serine deaminase (sdaA). We also found that undegraded alanine and serine inhibit the growth of ***BCG*** through blockage of glutamine synthetase. These results suggest that ***BCG*** strains are limited in nitrogen metabolic capacity and predict defects that may restrict multiplication and persistence of the live vaccine. . .

CT *Alanine: ME, metabolism
 Alanine Dehydrogenase
 Amino Acid Oxidoreductases: GE, genetics
 Amino Acid Oxidoreductases: ME, metabolism
 Animals
 ****BCG Vaccine***
 *** BCG Vaccine: GE, genetics***
 Cattle
 Culture Media
 Frameshift Mutation
 Glutamate-Ammonia Ligase: AI, antagonists & inhibitors
 *** L-Serine Dehydratase: GE, genetics***
 *** L-Serine Dehydratase: ME, metabolism***
 Molecular Sequence Data
 *Mycobacterium bovis: EN, enzymology
 *Mycobacterium bovis: GE, genetics
 Mycobacterium bovis: GD, growth & . . .

CN 0 (***BCG*** Vaccine); 0 (Culture Media); EC 1.4.- (Amino Acid Oxidoreductases); EC 1.4.1.1 (Alanine Dehydrogenase); EC 4.3.1.17 (***L*** - ***Serine*** ***Dehydratase***); EC 6.3.1.2 (Glutamate-Ammonia Ligase)

=> S BCG and (medium(2w)serine)
 L12 0 BCG AND (MEDIUM(2W) SERINE)

=> S BCG and (medium(2w)alanine)

L13 2 BCG AND (MEDIUM(2W) ALANINE)

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 2 DUP REM L13 (0 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1965:92797 CAPLUS <<LOGINID::20080329>>

DN 62:92797

OREF 62:16651a-b

TI Biogenesis of the N-methyl group of pyocyanine

AU Sheikh, N. M.; MacDonald, J. C.

CS Natl. Res. Council Canada, Saskatoon

SO Canadian Journal of Microbiology (1964), 10, 861-6

CODEN: CJMIAZ; ISSN: 0008-4166

DT Journal

LA Unavailable

AB Pseudomonas aeruginosa was grown in a ***medium*** contg. L-
alanine, glycerol, MgSO₄, K₂HPO₄, FeSO₄, L-serine, D-quinic acid,
and distd. water. Addn. of L-methionine-methyl-14C or L-serine-3-14C
resulted in production of labeled pyocyanine. The Me C atoms of
methionine supplied 66% of the N-methyl C atoms of pyocyanine and were not
incorporated to any extent into the rest of the pyocyanine mol. This was
true even when the strain of P. aeruginosa didn't require an exogenous
source of methionine. The labeled C atoms of serine-3-14C were
incorporated to a lesser extent and less specifically into the N-methyl C
atoms of pyocyanine.

AB Pseudomonas aeruginosa was grown in a ***medium*** contg. L-
alanine, glycerol, MgSO₄, K₂HPO₄, FeSO₄, L-serine, D-quinic acid,
and distd. water. Addn. of L-methionine-methyl-14C or L-serine-3-14C
resulted in production of labeled. . .

IT 54-85-3, Isonicotinic acid, hydrazide
(electrolyte metabolism by Mycobacterium ***BCG*** and)

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1964:434495 CAPLUS <<LOGINID::20080329>>

DN 61:34495

OREF 61:6069a-b

TI The occurrence of muramic acid in wax D preparations of mycobacteria

AU Stewart-Tull, D. E. S.; White, R. G.

CS London Hosp., UK

SO Journal of General Microbiology (1964), 34, 43-9

CODEN: JGMIAN; ISSN: 0022-1287

DT Journal

LA Unavailable

AB Acid hydrolyzates of wax D prepns. from human and bovine strains of M.
tuberculosis (grown for 4 weeks on Sauton ***medium***) contained
alanine, glutamic acid, and meso-.alpha.,.epsilon.-diaminopimelic
acid. Muramic acid was found in the wax from human strains but not in
that from bovine strains.

AB Acid hydrolyzates of wax D prepns. from human and bovine strains of M.
tuberculosis (grown for 4 weeks on Sauton ***medium***) contained
alanine, glutamic acid, and meso-.alpha.,.epsilon.-diaminopimelic
acid. Muramic acid was found in the wax from human strains but not in

that from. . .

IT Waxes or Waxy substances
(of Mycobacterium tuberculosis and M. tuberculosis ***BCG*** ,
muramic acid in D)